Understanding the Impact of Disability on Dietary Intake and Patterns in People with Multiple Sclerosis

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Abstract

As current treatments for multiple sclerosis (MS) do not prevent the accumulation of long-term disability, researchers and persons with MS are interested in wellness behaviours and how they may be used to manage MS. This thesis includes a review of the literature on wellness-based interventions in persons with progressive MS. Following this review, a cross-sectional study was conducted to characterize dietary intake by disability status in this population, and to examine the functional and symptomatic correlates of dietary behaviours. Participants with MS and matched controls completed questionnaires and a three-day food intake record. There were significant differences in dietary intake with and without supplements between the MS and control groups. Correlates of dietary behaviours were also examined. Further research examining dietary intake in MS is necessary to understand how disability and other factors impact dietary intake behaviours, and which other correlates may be useful targets for future nutrition interventions.

Puisque les traitements pour la sclérose en plaques (SP) ne préviennent pas l'accumulation de l'handicap à long terme, les chercheurs et les personnes avec la SP sont intéressés aux comportements de bien-être et leur utilité pour gérer la maladie. Cette thèse inclut une revue de littérature sur les interventions centrées sur le bien-être pour les gens avec la SP progressive. Suite à cette revue, une étude a été effectuée pour caractériser l'apport nutritionnel par niveau d'handicap dans cette population. Les participants avec la SP et contrôles ont complété des questionnaires et un journal alimentaire de 3 jours. Des différences ont été observées entre les groupes SP et le groupe contrôle pour les apports avec et sans suppléments. Des variables corrélées aux comportements alimentaires ont aussi été examinées. Des études futures examinant l'apport alimentaire des gens avec la SP sont nécessaires pour comprendre l'impact de ce handicap et d'autres facteurs sur ces comportements alimentaires.

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List of acronyms and abbreviations

AI	Adequate intake
BMI	Body mass index
CAM	Complementary and alternative medicine
CDSES	Cardiac diet self-efficacy scale
CNS	Central nervous system
DHQ	Diet history questionnaire
DMT	Disease modifying therapy
DRI	Dietary reference intake
EDSS	Expanded disability status scale
EER	Estimated energy requirements
GLTEQ	Godin leisure time exercise questionnaire
HADS	Hospital anxiety and depression scale
LLFDI	Late-life function and disability instrument
MFIS	Modified fatigue impact scale
MS	Multiple sclerosis
MSSS	Medical outcome study social support survey
MSWS	Multiple sclerosis walking scale
NARCOMS	North American Research Committee on Multiple Sclerosis
PDDS	Patient determined disease steps
PDQ	Perceived deficits questionnaire
PPMS	Primary progressive multiple sclerosis
PUFA	Polyunsaturated fatty acids
RDA	Recommended dietary allowance
RRMS	Relapsing-remitting multiple sclerosis

SACQ	Self-administered comorbidities questionnaire
SCT	Social cognitive theory
SPMS	Secondary progressive multiple sclerosis

Chapter 1

Review of Current Literature

1.1 INTRODUCTION

Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system (CNS) that is characterized by inflammation, demyelination, and neurodegeneration (1). MS affects approximately 2.5 million people worldwide, and it is the most common neurological cause of disability among young adults (2). In the initial stages of MS, neurons in the CNS are targets of inflammatory attacks that result in damage to both the myelin sheath and nearby oligodendrocytes, which are responsible for developing and repairing the myelin sheath. As these inflammatory attacks continue, they create irreversible damage to the CNS (3). The location and extent of damage within the CNS results in a variety of impairments and symptoms that typically worsen with disease progression (4). Psychological symptoms of MS can include fatigue, depression, anxiety, and cognitive impairment (5–15). Persons with MS also experience physical symptoms such as mobility impairment, spasticity, visual disturbances, muscle weakness, ataxia, balance impairments, and dysphagia (16–18). Collectively, these symptoms and impairments can negatively influence participation in daily activities and overall quality of life (QoL) (16,18). The later stage of MS is often characterized by a shift in disease pathology. While the frequency of inflammatory attacks on the CNS decreases, immune cells continue the deterioration of the myelin sheath which results in elevated, chronic neurological inflammation leading to neurodegeneration (3). Therefore, this shift in disease pathology (i.e., inflammatory to neurodegenerative), ultimately results in greater disability and impairment (3).

Geography is an important environmental risk factor to consider in the development of MS. Indeed, the prevalence of MS is greatest in the northern hemisphere, where it varies considerably (19). The highest prevalence is estimated at 1 in every 385 individuals, as currently reported in Canada (2). Overall, it is the highest in North America and Europe (>100/100,000 inhabitants), and it is much lower in East Asia and sub-Saharan Africa (2/100,000 inhabitants) (20). These

differences suggest that environmental factors may play a role in MS development. One environmental factor that has been suggested as a reason for the increased prevalence of MS in northern countries is lower levels of sunlight-based vitamin D with increasing latitude (19). Individuals who reside in northern countries will have overall less exposure to sunlight-based vitamin D, and this could increase their risk of developing MS. Other proposed environmental risk factors for MS include smoking, viruses and infection (20).

There are also genetic factors that contribute to MS development. First, sex is considered to be related to MS development, as it affects women two-three times more frequently than men (21). Second, ethnicity is another risk factor that is considered to play a role in the development of MS. A higher prevalence of MS has been observed in non-Hispanic whites than in other ethnic groups (21); however, certain studies have reported a higher prevalence among African Americans (22). Third, many genes that are thought to increase the predisposition for certain individuals to develop MS have been identified (23).

MS can be distinguished by three main clinical courses with different underlying disease pathologies: relapsing remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS) (24). The RRMS course is characterized by exacerbations of disease activity and symptoms (i.e., relapses) which are followed by partial or total recovery (25). PPMS is characterized by continuous accumulation of neurological disability following diagnosis, typically without relapses, and occurs from onset in around 20% of people with MS (24). Approximately half of patients with RRMS will develop into SPMS within ~10-20 years from diagnosis (26). SPMS is characterized by the continuous accumulation of neurological disability typically without relapses, preceding a RRMS course (24,27). At present, there is currently no cure for MS (28), and there are currently no treatments that prevent the accumulation of disability long-term (29). Most disease modifying therapies are currently approved for patients with RRMS, and have been shown to decrease the rate and severity of relapses (29,30). These therapies have largely been ineffective in managing the progressive course of MS, likely due to differences in underlying

disease pathology (i.e., inflammatory vs. neurodegenerative) (29,30).

1.2 PROGRESSIVE MS

It has been reported that patients with progressive courses of MS tend to experience irreversible disability sooner than those with a relapsing-remitting course at disease onset (31). There are also differences in disability progression between PPMS and SPMS, both with disability progression and symptom severity (32). For example, studies have shown that patients with SPMS would have a slower onset of disability than those with PPMS, however they would also present with faster disability progression (31,32). Further, when compared with RRMS patients, patients with PPMS experience more common and more severe fatigue (33,34). While there are disease-modifying therapies that reduce relapse rate and associated disability approved for RRMS, there is a lack of available treatment options for patients with progressive MS (35,36). There has been a recent focus on identifying solutions for the progressive course of the disease.

1.3 DISABILITY

Clinical disability in MS is most commonly measured with the Expanded Disability Status Scale (EDSS) (37), which is designed to quantify neurological disability in this population. This scale assesses seven functional systems including visual, brainstem, pyramidal, cerebellar, sensory, bladder and bowel, and cerebral, as well as ambulatory abilities. The scores from all functional systems are combined to give an EDSS score ranging from 0 (no disability) to 10 (death). Specific EDSS scores are indicative of levels of disability in persons with MS. Specifically, ranges of 0.0 – 3.0, 3.0 – 5.5, and 6.0 – 9.5 are considered to indicate mild, moderate, and severe disability, respectively. Patients with MS who are in the mild disability range show minimal physical impairments, but can experience other symptoms that are associated with MS, such as fatigue, vision and sensory impairments. Moderate disability is characterized by a greater impact of symptoms associated with MS, and the experience of gait impairment without the required use of

an assistive device for ambulation. Severe disability is associated with the necessary use of assistive devices for ambulation and can be further subdivided into unilateral assistance (6.0), bilateral assistance (6.5) and wheelchair dependence (7.0). Scores ranging from 7.5 to 9.5 are associated with immobility and bed rest (37).

Another scale that has been used to measure disability in MS is the Patient Determined Disease Steps Scale (PDDS). The PDDS is a patient-reported measure focusing on walking ability for which scores range from 0 (normal) to 8 (bedridden). PDDS scores are highly correlated with EDSS scores, and can be used to quantify disability (38). Specifically, scores ranging from 0.0 – 3.0 are indicative of mild disability, and are associated with having no gait impairment. PDDS scores 4.0 – 5.5 are indicative of moderate disability and are associated with early gait impairment. PDDS scores of 6 and greater are indicative of severe disability and are associated with assistive devices for ambulation, and immobility (39). PDDS scores correlate strongly (r=.93; ρ = .783) with EDSS scores, and can also be converted into EDSS scores (38).

1.4 WELLNESS AND MULTIPLE SCLEROSIS

Due to the incomplete efficacy of disease-modifying therapies, and the inability of these approaches to prevent disability accumulation long-term, there has been increasing interest in alternative strategies for disease management (40). Specifically, there has been a recent focus on wellness behaviours and approaches for managing MS (40). According to the National Wellness Institute, wellness is a process requiring active implication through which people increase their awareness and choices towards a healthier existence (41). The effort to increase wellness research in MS has largely been driven by input from people living with the disease. A social media listening survey was conducted that revealed wellness and related behaviours are a high priority for people living with MS (40). Persons with MS noted that they were particularly interested in how diet could help in managing their MS symptoms (42). Similarly, over one thousand Canadians living with MS participated in the 'MS Wellness Survey' conducted by the MS

Society of Canada in 2015, in which physical activity and exercise, emotional well-being (e.g., stress management and mindfulness), and diet and nutrition were identified as areas of interest and research priority by persons living with MS (43). In regards to diet and supplements, surveyed individuals with MS were specifically interested in how diet and supplements affect the disease course and symptoms, in the development of resources to provide meal plans, recipes, and advice for food preparation, and in the improvement of financial access to affordable and healthy foods (43). Recent studies on alternative strategies for disease management (i.e., dietary modification) in MS have highlighted that the use of these strategies may be higher in people with MS than in the general population (44,45), where 77.1% of persons with MS reported using alternative strategies for disease management within the past twelve months (45). Studies focusing specifically on the use of dietary supplements reported that food supplements, vitamins, and minerals are used by 64.7% of people with MS (46). One study investigating the use of alternative strategies for disease management in persons with MS found that 11.9% of participants were undergoing dietary intervention as well as taking supplements (47). Another study reported that 29.6% of people with MS used diet-based therapies, and 88.9% of participants took vitamin and mineral supplements (45). These values differ from those reported in the general Canadian population. A survey conducted in 2015 by Statistics Canada found that 45.6% of Canadians aged one year and older take at least one nutritional supplement (48).

1.5 DIET AND MULTIPLE SCLEROSIS

Despite patient interest and use of dietary modification and/or supplements, research regarding the role of diet in MS has been conflicting. A recent systematic review on the influence of diet in MS retrieved 27 clinical trials and 20 observational studies (46). Much of this research has focused on the role of diet in the development, progression, and treatment of the disease. There are conflicting findings regarding the link between dietary intake and MS prevalence, or the risk of developing MS. Some studies have reported that the intake of fruit, low fat-dairy, whole

grains, legumes, vitamin D, and fish intake are associated with a reduced risk of developing MS (49–52), and that increased intake of sugar, animal fat, and vegetable oil could increase the risk of developing MS (49,50). Other studies have found no relationship between the intake of alcohol, caffeine, vitamin D, and vitamin B-12 and the risk of developing MS (53–55).

There is some evidence for the relationship between diet and disease activity and progression in MS. One study investigating the perceived link between nutrition and lifestyle factors and disease activity found that persons with MS have linked certain nutrition and lifestyle factors to their disease activity (56). The perceived nutrition factors identified as negatively impacting disease were the intake of sugar, red meat, fast food, fatty food, and alcohol (56). The perceived nutrition factors that were identified as positively impacting disease were the intake of fish, vegetables, and dietary supplements and vitamins (56). Some cross-sectional studies have found that higher fruit, vegetable, unsaturated oil, vitamin B12, antioxidant supplements, fish, omega-3 supplements, and cod liver oil intake are linked with reduced disease activity and disability (57–60), while high sodium intake has been linked with increased disease activity in MS (61). Clinical trials examining how diet might impact MS disease activity have found that PUFA supplements, antioxidant supplements, fish oil, high doses of vitamin D, and low-fat dietary intake tend to result in fewer relapses (62–66). A recent study reported that the combination of omega-3 fatty acids and vitamin D_3 supplementation had beneficial effects on disability scores and on inflammation and antioxidant capacity, glycemic control, insulin sensitivity, and lipid profiles of people with MS (67). Other trials have found no link between vitamin D and vitamin A intake and MS relapse rate (68,69). Overall, the current literature regarding diet and disease progression in people with MS is limited, and it is difficult to associate or recommend any specific diet with therapeutic effects at this time (46). Although limited, there has also been interest in characterizing dietary patterns and intake in people with MS. For example, one study examining dietary intake in newly diagnosed persons with MS (ages 20-55, 59% women, EDSS m = 2, SD = 1.72) found that carbohydrate, fat, and protein intakes were 46.9%, 38.4%, and 14.6% of total daily energy intake,

respectively (58). The Acceptable Macronutrient Distribution Ranges for healthy adults from the Dietary Reference Intakes recommend that the dietary intakes of carbohydrates, fat, and protein represent 45-65%, 20-35%, and 10-35% of total daily energy intake, respectively (70). Another study with persons with MS observed that recommended daily intake (RDI) values were not met for protein, carbohydrate, polyunsaturated fat, and dietary fiber intakes, and that the intake of saturated and total fat was higher than recommended values (71). To compare these results with the general population, the 2004 Canadian Community Health Survey focusing on nutrition highlighted that while Canadian adults consume protein in quantities that meet RDI, only a smaller proportion consume carbohydrates and fat in quantities that meet RDI (72). Specifically, carbohydrate intake tends to be below RDI, and fat intake tends to be above RDI for Canadian adults (72). In a study examining the intake of thirteen nutrients in MS, intake of five nutrients (carbohydrates, dietary fiber, vitamin E, calcium, and zinc), reached 90% of RDI, while intake of six other nutrients (saturated fat, protein, vitamin A, vitamin C, folate, and iron) were consumed in higher levels, reaching 10% over RDI (73). Another study investigating multiple risk factors in MS including diet reported that 85.5% of participants did not meet recommended nutrient intake guidelines (74). While malnutrition (i.e., nutritional intake characterized by deficiencies, excesses, or imbalances) (75) has not been extensively examined in persons with MS, some studies have reported that malnutrition may be more frequent among people with MS than in other chronic neurological diseases, including headaches, vertigo, carpal tunnel syndrome and lumbar discopathy (76).

Disease-related factors may further influence dietary patterns and behaviour in people with MS. Some factors that are known to influence dietary behaviours in the general population are personal characteristics (e.g., age, sex, education level) (77), psychosocial factors (e.g., self-efficacy, outlook on life) (78), and health status (e.g., cognitive impairment, mobility impairment, activity limitations) (79). In addition to these factors, other disease-related factors (e.g., fatigue, pain, difficulty swallowing) may make it increasingly difficult to acquire, prepare, and consume

healthy foods for persons with MS (80). For example, in one qualitative study conducted with people with MS experiencing mobility impairments, participants reported that fatigue and mobility impairment were barriers to dietary behaviours (e.g., preparing food, grocery shopping, and going to restaurants), and that their family members were sources of support to overcome these barriers (81). Few studies have examined correlates of dietary behaviours in people with MS. One study identified dietary self-efficacy, physician communication, and physical activity as significant predictors of healthy dietary behaviours in people with MS, whereas impairments (i.e., problems with body structures and functions) and activity limitations (i.e., difficulty with executing actions or tasks) were not significantly associated with dietary behaviours (82). Another cross-sectional study examined the relationship between diet, quality of life, disability, and relapse rate in persons with MS (57). This study reported that a healthier diet (i.e., higher intake of fruits, vegetables, and lower intake of dairy and meat) predicted better quality of life and lower levels of disability compared to an unhealthy diet (57). Participants with mild disability (i.e., PDDS scores 0-2) in that study were more likely to engage in healthy dietary behaviours compared to participants with moderate or major disability (i.e., PDDS scores 4.0 – 8.0) (57). Greater disability in MS is associated with an increased frequency and severity of symptoms and impairments (83). As such, it would be expected that disability status could influence engagement in health behaviours such as diet; however, these relationships have yet to be comprehensively examined.

1.6 SOCIAL COGNITIVE THEORY AND HEALTH BEHAVIOURS IN MS

Theoretical models and frameworks can provide guidance for understanding and changing health behaviours in a variety of settings. Social Cognitive Theory (SCT) proposes that changes in behaviour are made possible through a personal sense of control (84). That is, if individuals believe that they are capable to take action to solve a problem, they are more likely to do so, and to feel more dedicated to their choice (84). SCT is considered one of the most comprehensive behavioural change theories as it includes individual, social, and environmental factors (85). SCT

has been used in the prediction and study of many health behaviours, such as adherence to medication, exercise, addictive behaviours, and nutrition and weight control in various populations (86). The key constructs of the sociocognitive causal structure for health-promoting behaviors are self-efficacy, outcome expectations (i.e., physical, social, self-evaluative), sociostructural factors (i.e., facilitators, impediments), and goals as predictors of the behavior (see Figure 1) (87). Self-efficacy is an important predictor of various lifestyle behaviours, defined as the confidence that one can be successful in managing a challenging situation or completing a task (84,88). Self-efficacy has been associated with many health-related behaviours in people with MS specifically, including participation in physical activity (80,89,90), strategies for managing one's emotions, and dietary behaviours (80). To date, research examining physical activity and behavioural change theories in MS has largely focused on SCT, and the evidence from this research (i.e., cross-sectional, longitudinal, and experimental) supports the application of SCT as behavioural change theory in this population (91).

Self-efficacy and SCT have been used to understand and improve diet in the general population (92,93), in older adults (94), and in patients with heart disease (95). Findings in these areas highlight that self-efficacy is an important target of health behaviour change interventions, including dietary modification, and participants who received interventions focused on increasing dietary self-efficacy improved their dietary behaviours (i.e., consumed more fruits and vegetables, planned healthy eating, maintained dietary behaviour change) (92,94,95). Some studies have examined the cross-sectional association between dietary self-efficacy and dietary patterns in people with MS. These studies have reported conflicting findings. One study found no relationship between dietary self-efficacy and dietary intake (96). Two other studies reported a significant relationship between dietary self-efficacy and dietary patterns in people with MS (82), and in women with physical disabilities in which self-efficacy was the strongest predictor of dietary patterns (97). The discrepancies between these findings may be related to the different outcome measures that were used to assess dietary intake (e.g., 24 hours recalls, DHQ, and Nutritional

Patterns Scale).

Another important factor that may influence self-efficacy and engagement in health behaviours in people with MS is social support. Within the SCT sociocognitive causal structure, social support can be considered as a facilitator to engagement in a health behaviour. One study examining cross-sectional associations between self-efficacy and physical activity in MS highlighted that social support has a significant relationship with self-efficacy (98). In another study examining cross-sectional associations between self-efficacy, physical activity and dietary behaviours in women with physical disabilities, self-efficacy, social support, assistance with activities of daily living (ADL) and mobility were all identified as significant predictors of dietary behaviours (97). In another study, dietary self-efficacy and social support were not found to be significantly associated with engagement in health promoting behaviours such as diet (73).

1.7 RATIONALE AND STUDY OBJECTIVES

Most research on diet in MS thus far has focused on how diet can influence the risk of disease development and progression. However, few studies have specifically focused on understanding dietary patterns and intake within different MS subtypes (i.e., relapsing vs progressive MS). There has also been little emphasis on how the disease and consequent burden of disability impacts nutritional status in persons with MS. There has been a lack of examination of dietary patterns across the disability spectrum, particularly among persons with severe disability who may experience the greatest challenges and barriers to healthy eating. The relationships between MS impairments and symptoms such as physical and cognitive impairment, fatigue, anxiety, and depression with dietary patterns have also not been completely examined. Previous studies have used retrospective approaches for collecting dietary data, such as food frequency questionnaires and 24-hour recalls. Many studies have also used qualitative approaches with small samples to examine dietary behaviours. The application of a theoretical framework, such as SCT, would be useful to understand and explain the potential impact of disability on dietary

behaviours and to identify targets for nutritional interventions in persons with MS. A SCT framework would be the best fit for this study as it provides a complete, cohesive view of what might impact engagement in a health behaviour through its key constructs. Furthermore, it has been used most frequently to understand and change health behaviours in people with MS and in many other populations, and because much less is known about the application of other theories to understand health behaviours in people with MS (91).

The purpose of this thesis was twofold: (i) to summarize the current literature investigating wellness-based interventions, including diet, in persons with MS, with a specific focus on the progressive disease course; and (ii) to further characterize dietary patterns in people with MS and understand the potential influence of disability on these patterns. Lifestyle and wellness-based approaches may be most relevant for patients with progressive MS and/or severe disability, as there are currently limited disease-modifying therapies available for this segment of the MS population. Lifestyle-based interventions can be used to target and modify wellness behaviours, and may provide an alternative approach for managing various outcomes in patients with progressive and/or severe MS. This review will provide researchers and clinicians with direction on which lifestyle and wellness-based interventions are the most effective and feasible for patients with progressive MS.

The further characterization of dietary intake and patterns in people with MS is important in order to determine whether persons with MS consume a healthy diet meeting recommended daily intakes for all nutrients. It is particularly important to further characterize how disability and use of assistive devices for ambulation might impact dietary intake and patterns in people with MS, as persons with progressive courses of MS and severe disability, collectively, may experience the greatest barriers and challenges with healthy eating. It is also important to consider how the relationships between various factors such as disability, assistive device use, impairments and symptoms, and environmental factors might impact dietary intake in persons with MS. Overall, such a comprehensive exploration of these factors and their relationships will determine whether

they impact dietary intake in with persons with MS. The identification of specific barriers to healthy eating for persons with progressive MS and severe disability will be the first step leading to the elaborations of solutions to overcome them.

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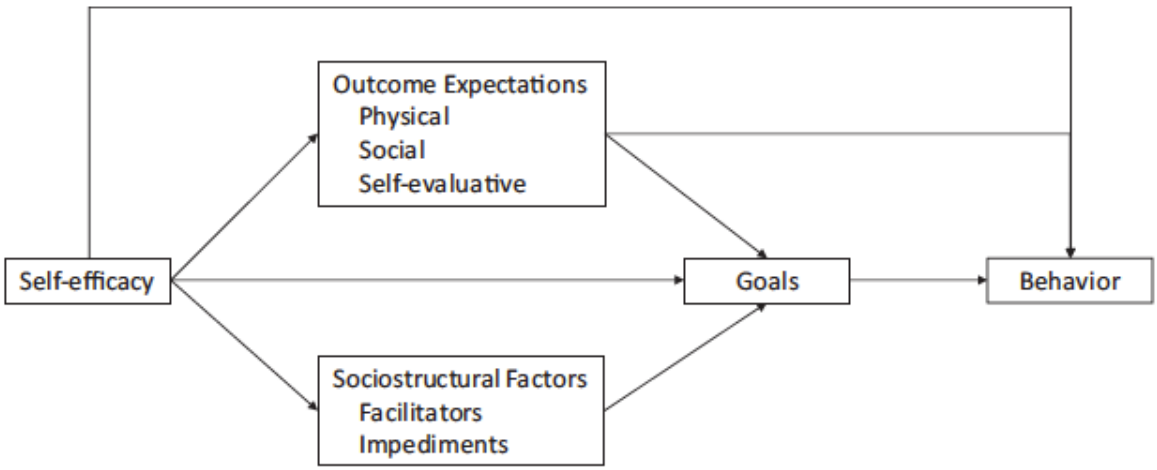
Chapter 1

Figures

Figure 1. Sociocognitive causal structures for health-promoting behaviours. Adapted from Bandura.



Chapter 2

Exploring Wellness Interventions in Progressive Multiple Sclerosis: An Evidence-Based Review

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Keywords: multiple sclerosis; progressive; wellness; exercise; mindfulness; diet

Preface: This article included collaboration between myself, Thomas Edwards, and my supervisor, Dr. Lara Pilutti. The literature review portion was divided equally among authors, with Dr. Lara Pilutti conducting a literature search for exercise interventions in progressive MS, Thomas Edwards conducting a literature search for dietary interventions in persons with progressive MS, and myself, conducting a literature search on emotional wellness interventions. The writing of the introduction, methods, results, and conclusions were shared by myself and Thomas Edwards, and were reviewed by Dr. Lara Pilutti.

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2.1 ABSTRACT

Purpose of review: There has been recent interest in the role of lifestyle and wellness-based approaches in the treatment and management of multiple sclerosis (MS). These approaches may be particularly relevant for patients with progressive MS, considering limited therapeutic options currently available. The purpose of this review is to examine the role of wellness-based interventions including exercise training, emotional well-being therapies, and dietary modification in patients with progressive MS.

Recent Findings: We conducted a literature search on the efficacy of wellness-based interventions in patients with progressive MS published between 1985 and July 2017. The level of evidence for each trial was evaluated using the American Academy of Neurology criteria. Overall, 21 articles reporting on 16 wellness-based interventions were identified: ten trials involved exercise training, three involved emotional wellness therapies, two involved dietary modification, and one was a combined wellness intervention.

Summary: There is level C evidence (possibly effective; one Class II study) for the efficacy of aerobic exercise training on cardiorespiratory fitness in patients with progressive MS. There is level B evidence (probably effective; one Class I study) for the efficacy of mindfulness training on psychological distress, depression, anxiety, pain, and quality of life in patients with progressive MS. There is inadequate evidence (level U) for efficacy of dietary modification (one Class III study and one Class IV study) and combined wellness interventions involving exercise training, meditation, and dietary modification (one Class IV study). High-quality research is needed to provide evidence-based recommendations for wellness behaviours and lifestyle change in patients with progressive MS.

2.2 INTRODUCTION

Multiple sclerosis (MS) is a chronic, neurological disorder of the central nervous system (CNS) that is characterized by inflammation, demyelination, and neurodegeneration [1]. The

clinical course of MS can be distinguished by the level of acute inflammatory disease activity vs. insidious progression; the two core phenotypes being classified as relapsing and progressive MS [2]. The progressive MS phenotype can further be subdivided into primary and secondary progressive MS [2]. Approximately 10-20% of patients are diagnosed with primary progressive MS (PPMS) at onset, which is characterized by gradual accumulation of neurologic disability over time without recovery [2, 3]. Approximately 50% of patients who initially present with relapsing-remitting MS (RRMS) will develop secondary progressive MS (SPMS), characterized by progressive accumulation of neurological disability following an initial relapsing course [2, 4, 5]. There are now many disease-modifying therapies approved for the treatment of relapsing MS that have been shown to reduce rate of relapses and associated disability [6, 7•]. Despite substantial effort, similar progress has not been made in the development of therapies for patients with progressive MS [6, 7•]. Recent initiatives such as the International Progressive MS Alliance [6, 8] and recommendations for progressive MS trials [7•] should ameliorate the treatment landscape moving forward; however, the role of lifestyle modification in the management of patients with progressive MS should also be considered.

There has been a recent focus on increasing our understanding of lifestyle practices and wellness behaviours in the treatment and management of MS [9•]. This interest likely stems from the incomplete efficacy and side-effects associated with disease-modifying therapies, growing evidence for the prevalence and impact of comorbid health conditions, as well as input from patients living with the disease [9•–12]. For instance, a social media listening study reported that wellness and related behaviours are a high priority for people living with MS [11]. These findings lead to the development of the MS Wellness Research Working Group to establish specific priorities and directions for wellness research in MS [9•]. Similarly, 1,082 Canadians living with MS participated in the MS Wellness Survey conducted by the MS Society of Canada, in which current wellness behaviours and gaps in wellness research were highlighted [11, 12]. Collectively, the three wellness areas identified in both reports were physical activity and exercise, emotional

well-being (e.g., stress management and mindfulness), and diet and nutrition [11, 12]. Lifestyle-based interventions can be used to target and modify wellness behaviours, and may provide an alternative approach for managing various outcomes in patients with progressive MS.

This review explores the role of wellness-based interventions in patients with progressive MS by providing a summary of the current evidence for the efficacy of exercise training, emotional well-being therapies, and dietary modification. We conducted a literature search of five electronic databases (PubMed, EMBASE, Web of Science, OvidMEDLINE, and PsychINFO), the authors' personal libraries, and reference lists of relevant systematic reviews and meta-analyses. Studies included in the review involved patients with PPMS or SPMS who participated in a wellness-based intervention of exercise training, emotional well-being, or dietary modification, and were published in English between 1985 and July 2017. The literature search terms were as follows: *multiple sclerosis* AND *progressive* OR *severe* OR *disability* AND *wellness* OR *exercise* OR *physical activity* OR *training* OR *rehabilitation* OR *mindfulness* OR *stress management* OR *cognitive behavioral therapy* OR *diet* OR *nutrition* OR *intake.* The level of evidence was rated for each study using the American Academy of Neurology criteria [13] and feasibility metrics including patient retention, adherence, and adverse events were summarized. The final search retrieved 21 articles that reported on 16 studies of wellness-based interventions in patients with progressive MS (Table 1); ten studies examined exercise training, three examined emotional well-being therapies (primarily mindfulness), two examined dietary modification, and one was a combined wellness intervention (i.e., involved more than wellness component). Considering the limited number of records identified, the focus of this review will be primarily on exercise training, with an exploration of mindfulness, dietary modification, and combined wellness therapies for patients with progressive MS.

2.3 WELLNESS INTERVENTIONS

2.3.1 Exercise Training

Exercise is considered a subset of physical activity that is defined as planned, structured, and repetitive bodily movement done with the intention of improving or maintaining one or more component of physical fitness (i.e., cardiorespiratory fitness, muscular fitness, or body composition) [14]. There is now substantial evidence for the benefits of exercise training in persons with MS that is derived from several systematic reviews and meta-analyses [15•]. Overall, exercise training has been associated with small-to-moderate effects on physical fitness, mobility, balance, fatigue, depression, and health-related quality of life [16–26•]. This evidence supported the development of MS-specific physical activity guidelines which recommend two weekly sessions of moderate intensity aerobic activity and two weekly sessions of strength training activities for adults with minimal to moderate disability [16, 26•]. Despite these benefits and recommendations, the current evidence for exercise training in patients with MS is limited primarily to people with relapsing MS, or samples with mixed disease courses (i.e., progressive and relapsing MS). Few trials have focused on the role of exercise training in patients with progressive MS specifically.

The present literature search retrieved 11 articles involving 10 trials of exercise training in patients with progressive MS (Table 1). These interventions ranged between 4 to 24 weeks in duration and in most cases exercise was performed 2-3 times per week. The exercise modalities used were primarily specialized exercise equipment and involved aerobic exercise (e.g., arm ergometer; n=3 studies), body-weight supported treadmill walking (n=4 studies), electrical stimulation assisted cycling or function electrical stimulation cycling (n=3), recumbent stepping (n=1), and group-based aquatic exercise (n=1). The use of specialized, physically accessible equipment is likely a reflection of the level of disability of the samples, such that mean EDSS score in most trials was ≥ 5.0 (i.e., disability severe enough to impair ambulation and full daily activities).

There was one Class II RCT [27••, 28] involving 42 patients with progressive MS who were randomized to one of three aerobic exercise modalities (arm ergometry, rowing, and leg cycle ergometry) or a wait-list control condition. Overall, aerobic exercise training resulted in a significant improvement in cardiorespiratory fitness, walking endurance, depressive symptoms, fatigue, and

some test of cognitive performance. Furthermore, there was one Class III RCT [29•] of upper body aerobic exercise training that also supported improvements in cardiorespiratory fitness, although this change was not statistically significant (p=.06). The remaining studies were Class IV [30-37] and reported mixed findings for the role of exercise training in patients with progressive MS, most likely due to the low quality of the trial designs. Overall, these studies reported significant improvements in thigh circumference, walking speed and endurance, gait, acute spasticity, fatigue, and quality of life (QoL) [30–34, 37]. Several trials further reported non-significant improvements in muscle strength, walking speed and endurance, agility, balance, spasticity, fatigue, QoL, MSFC scores, and self-reported leg circulation and transfer ability [30–33, 35, 36]. None of the studies reported a change in EDSS score following exercise training [29•, 30, 33], and others reported no change in MSFC scores, spasticity, and some QoL scales [29•, 31, 32, 34–37], suggesting conflicting evidence for these outcomes.

Collectively, the current research involving exercise training in patients with progressive MS resulted in a level C classification (i.e., possibly effective) for the efficacy of aerobic exercise training on cardiorespiratory fitness. This may be particularly relevant for patients with progressive MS, as levels of physical fitness, including cardiorespiratory fitness, have been shown to decline with disease and disability progression [19, 38, 40]. Such loss may be counteracted or slowed with aerobic exercise training. Cardiorespiratory fitness has further been associated with mobility, symptomatic outcomes, cognitive performance, brain structure on MRI, body composition, activities of daily living, and QoL in patients with MS overall [38, 40–43], highlighting the importance of this outcome.

Although there was evidence from one Class II study [27••] for the efficacy of exercise training on other outcomes including mobility, symptoms, and participatory measures, conflicting evidence from one Class III [29•] and eight Class IV trials [30–37] resulted in a level U classification overall (i.e., data inadequate or conflicting). At this time, there is insufficient, high-quality evidence to make recommendations for the efficacy of exercise training on other outcomes in patients with

progressive MS. Notable limitations of this body of work include the small sample sizes, heterogeneity in patient characteristics and exercise prescriptions, lack of specification of primary outcomes, and lack of patient samples pre-selected for outcomes interest.

Increasing participation in exercise and physical activity might be particularly important for patients with progressive MS due to low levels of physical activity in this group [44]. Indeed, lower levels of physical activity have been reported in patients with MS compared to people without MS, and patients with progressive MS, in particular, participate in even less physical activity than patients with relapsing MS [44–46]. This highlights the need for exercise training interventions that target patients with progressive MS specifically.

With respect to feasibility metrics, patient retention was reported on in all trials, with drop-out rates ranging between 0% and 39% (Table 2). The interventions with the highest rate of drop-out included aquatic exercise (39%) [37] and electrical stimulation assisted cycling (33%) [34]. These drop-out rates are comparable to those reported in a systematic review of the safety of exercise training in patients with MS (mean=15.5%; range=0% to 37.5%) which involved primarily relapsing or mixed MS samples [47]. Overall adherence with the prescribed exercise protocol was reported on in three trials and ranged between 89% and 98%, suggesting good compliance with upper body aerobic exercise, recumbent stepper training, and body-weight supported treadmill walking. Adverse events were reported from five exercise trials; one study reported no adverse events and four reported non-serious events that were seemingly expected in response to exercise training or to the use of specialized exercise equipment, or were reported as unrelated to the intervention. There is promising evidence for the feasibility of exercise training in patients with progressive MS; however, incomplete reporting of these metrics limit the ability to provide conclusive recommendations at this time.

2.3.2 Emotional Well-being

Emotional wellness is defined as a process that includes awareness, expression, and management of emotions in a continuous manner [48]. It also involves keeping all self-assessments realistic and an overall positive approach to life and towards one's self [48]. Emotional wellness interventions can include various components, such as optimistic outlooks on one's self and life, self-awareness, stress management, and mindfulness training [49]. There has been increasing interest in the role of mindfulness therapies in the management of various chronic health conditions, including MS [50]. Mindfulness has been defined as the action of purposefully paying attention in the present moment in a non-judgemental manner [51]. To date, there is one systematic review of mindfulness-based therapies in patients with MS [52•]. This review reported potential benefits of mindfulness-based interventions on symptomatic, mental health, and QoL [52•]; however there were only three studies included in this review and most patients had a diagnosis of relapsing MS (67%). Recently published studies have further reported benefits of mindfulness-based interventions on psychological (i.e., self-compassion, acceptance, and stress), social (i.e., relationships), and physical health outcomes (i.e., walking and sleep) [53], as well as symptoms of depression and anxiety [54]. Having greater trait mindfulness in patients with relapsing MS has been associated with lower psychological stress, greater resilience, and better coping skills and overall QoL [55]. While the results from these studies are promising, the lack of patients with progressive MS in these trials makes it difficult to determine whether interventions targeting emotional well-being are also beneficial in progressive MS.

The present literature search retrieved four articles from three trials focused on emotional well-being in patients with progressive MS (Table 1). Overall, the interventions included primarily a mindfulness therapy delivered in-person or remotely over 8-10 weeks, and used individual as well as group-based approaches. One Class I RCT examined the efficacy of a group-based mindfulness intervention delivered via Skype™ on distress in 40 persons living with PPMS and SPMS [56••]. The intervention group reported significantly lower psychological distress, as well as reduced depression, anxiety, and pain, and improved psychological QoL immediately after the

intervention, and at 3-month follow-up, suggesting possible lasting effects of the intervention [56••]. Qualitative interviews were conducted with the mindfulness group for examining mediator variables of intervention effects [57]. This follow-up study reported that decentring (i.e., the perception of thoughts as not a direct reflection of reality) and self-efficacy were the strongest mediators of the change in distress post-intervention [57]. One Class III study examined if mindfulness of movement could improve symptom management through six in-person instructional sessions, with supplemental audio and video content encouraging body awareness, self-acceptance, and self-compassion [58]. The mindfulness group improved on outcomes of balance and symptom management [58]. One Class IV trial examined the efficacy of mindfulness-based cognitive therapy on fatigue in patients with progressive MS with severe fatigue [59]. The intervention resulted in a significant reduction in symptoms of fatigue, as well as depression, anxiety, cognitive symptoms, coping, and mindfulness [59]. Patient retention was reported in all mindfulness trials, with drop-outs ranging between 5 and 29% (Table 2). This rate is similar to those reported in other mindfulness-based interventions in samples with primarily relapsing MS [52•]. The intervention with the highest rate of drop-out also reported symptoms of fatigue and exacerbation of MS symptoms as adverse events [59]. The other three studies did not report on adverse events.

Collectively, the current research involving mindfulness interventions in patients with progressive MS resulted in a level B classification (i.e., probably effective) for the efficacy of mindfulness-based training on psychological distress, depression, anxiety, pain, and QoL. These findings are promising considering that patients with progressive MS often experience greater prevalence and severity of symptoms compared to those with relapsing MS. For instance, symptoms of depression have been reported to be significantly higher in patients with SPMS compared to those with RRMS [60]. Symptoms of fatigue affect approximately 50-80% of patients with MS [61–63], and fatigue has been reported more frequently by persons with progressive MS [64–66]. Further, cognitive dysfunction is more prevalent and more severe among patients with

SPMS [67]. Previous studies have reported that patients with SPMS present with significant impairments in information processing speed and working memory when compared to patients with RRMS [68]. Collectively, this emphasizes the importance of identifying alternative and/or adjuvant therapies, such as mindfulness training, for symptom management in patients with progressive MS [69].

2.3.3 Dietary Modification

There has been a longstanding interest in the potential therapeutic role of diet for patients with MS; however, few high-quality trials of dietary interventions have been conducted [70•–72]. Specific dietary interventions have focused primarily on the modification of macronutrient consumption (e.g., low-fat diets), and/or dietary supplementation (e.g., fatty acids, antioxidants, and vitamins) [70•, 71, 73]. Some of the earliest evidence on diet in patients with MS comes from a 34-year, prospective trial that examined a low saturated fat diet (<10–15 g/day) with polyunsaturated fatty acid (PUFA) supplementation, commonly referred to as the 'Swank diet' [74]. This study reported lower rates of mortality and levels of disability among patients who were classified as "good dieters" (FAT <20g/day) compared to "poor dieters" (FAT >20 g/day) over the study period; however, there are a number of methodological limitations of this trial including the lack of a control condition and randomization. The safety and efficacy of dietary interventions with PUFA supplementation have since been examined in a systematic review involving 794 patients with MS from six RCTs [73], and this review reported no effect of PUFA supplementation on disease progression. The overall quality of the trials reviewed was considered poor with insufficient data to make recommendations regarding the safety of PUFA supplementation in MS. Two systematic reviews have been published recently on the role of dietary interventions in patients with MS [70•, 71]. These studies reinforce the lack of high-quality research, and do not definitively support a specific diet for patients with MS. Further, this literature has focused primarily on patients with relapsing MS.

The current search identified two studies examining dietary interventions in patients with progressive MS [75•, 76]; both trials involved dietary modification with supplementation (Table 1). One Class III randomized, placebo-controlled trial examined a 42-day, low-fat diet (≤ 30% of caloric intake) with antioxidant supplementation (200 mg/day of Lipia citriadora) compared to a low-fat diet alone on biochemical, inflammatory, and oxidative stress markers [75•]. Most notably, this study reported significantly lower C-reactive protein concentrations and higher catalase antioxidant activity in the low-fat diet and supplement group compared to the diet-only group, suggesting an overall decrease in inflammatory activity [75•]. The other study (Class IV) examined the effects of a 6-month, calorie-restricted (1700-800 kcal/day), modified Mediterranean diet (semi-vegetarian, preference for fish over meat, and low gluten) with dietary supplements on inflammatory markers [76]. Patients were also recommended to participate in physical activity (20–30 min, twice daily); however, it is unclear if this was completed as physical activity levels were not reported in the trial. Matrix metalloproteinase-9 levels (a mediator of inflammation) decreased by 59% after the intervention, however, no statistical analyses were performed. A small, non-significant decrease in fatigue, waist and hip circumferences, and body weight were reported.

With respect to feasibility, no drop-outs or adverse events were reported from the Class III study [75•], while the Class IV study [76] reported a dropout rate of 20% (Table 2). Neither study reported on adherence with the specific dietary protocols prescribed. The current research involving dietary interventions in patients with progressive MS resulted in a level U classification (i.e., data inadequate or conflicting) for the efficacy of dietary modification with supplementation. Consistent with the larger evidence-base on dietary interventions in MS, there is inadequate evidence to make specific dietary recommendations for patients with progressive MS at this time.

Few studies have examined differences in dietary intake or patterns by clinical disease course in patients with MS. One study reported that patients with SPMS had a lower intake of magnesium, calcium, and iron compared to those with PPMS and benign MS (defined as EDSS score ≤3.0, disease duration ≥10 years, and without disease progression) [77]. Another study

reported no differences in saturated and unsaturated fatty acid or PUFA intake by disease course [78]. It is also important to consider the potential impact of disability status on dietary behaviours and health consequences. As individuals with progressive MS typically experience greater disability burden [79], processes of acquiring, preparing, and consuming food may be more challenging [80]. Indeed, significant associations have been established between self-reported disability status and dietary habits, such that lower disability levels were associated with more healthy dietary habits (e.g., greater consumption of fruits, vegetables, and healthy fats) [72]. Recent research has reported no differences in body composition of ambulatory patients with progressive versus relapsing MS [81]; however, others have reported negative associations between disability status and bone mineral content and lean tissue mass in patients with MS [82]. Dietary modification and/or supplementation might be one approach for counteracting bone and muscle loss in patients with MS who experience these health conditions. Further research is needed to characterize dietary behaviours, nutrient intake, and associated health consequences in patients with progressive MS to inform targeted dietary interventions for this group.

2.3.4 Combined

The present literature search retrieved four articles reporting on various aspects from one Class IV trial [83–86] involving a combined wellness intervention in patients with secondary progressive MS (Table 1). The multimodal intervention involved 12-months of exercise training (trunk and lower extremity stretching and strengthening), meditation (daily breathing sessions), self-massage (hands, feet and face), and dietary modification (Paleolithic diet with nutritional and antioxidant supplementation). Significant improvements were reported in fatigue [83–85], QoL [85], depression [86], anxiety [86], and cognitive performance (i.e., language, switch, similarities, and matrix reasoning) [86]. High rates of retention (80-90%) and good adherence with the exercise (>70%) and dietary (>90%) components of the intervention were reported (Table 2) [83, 86], suggesting that a combined wellness intervention may not be more burdensome for patients. The

adverse events reported included minor gastrointestinal distress, skin irritation, headache, irritability, and fatigue [83–86]. The single trial was Class IV, resulting in a level U recommendation (i.e., data inadequate or conflicting), for the efficacy of combined wellness therapies. Further trials are needed to determine the potential added benefits and burden of combined wellness approaches for managing progressive MS.

2.4 CONCLUSIONS

As progressive MS remains one of the greatest therapeutic challenges, lifestyle modification should be considered within the current continuum of patient care. Current evidence suggests possible benefits of exercise training and mindfulness therapies for patients living with progressive MS, although this literature is limited. There in an inconclusive evidence for specific dietary modification or combined wellness interventions. Collectively, the current level of evidence points to the need for high-quality research to determine the feasibility and efficacy of wellness-based approaches in progressive MS. Better characterization of wellness behaviours in progressive MS will be critical to design, test, and implement the most effective therapies for patients living with progressive MS.

2.5 COMPLIANCE WITH ETHICS GUIDELINES

Myriam Venasse and Thomas Edwards declare no conflicts of interest. Lara Pilutti reports receiving research grants from the National Multiple Sclerosis Society and the Consortium of Multiple Sclerosis Centers outside of this work.

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Chapter 2

Tables

Table 1. Study design, sample characteristics, and results of wellness-based interventions in patients with progressive MS.

	Study Design			Sample Characteristics			Results
Reference	**Design (AAN Class)**	**n**	**Intervention**	**EDSS**	**Disease Duration (y) Mean ± SD**	**Age (y) Mean ± SD**	**Study Findings**
Exercise Training							
[27••, 28]	RCT (II)	32	8-10 weeks, AET				*↑ CRF (VO_{2peak}), walking endurance (6MW), cognition (attention, tonic alertness, verbal learning) *↓ Depression (IDS), fatigue (MFIS) *↑ Serum BDNF (acute exercise response) ↔ Serum Irisin, IL-6 (acute exercise response) ↔ Serum BDNF, Irisin, IL-6 (post-intervention)
			Arm-cycle ergometer	5.2±0.9	17.1±7.2	49.1±8.5	
			Rowing	4.7±0.8	14.1±6.1	50.9±9.2	
			Leg-cycle ergometer	5.0±0.8	13.3±5.4	48.8±6.8	
		10	Waitlist control	4.9±0.9	18.9±9.8	50.4±7.6	
[29•]	RCT (III)	6	4 weeks, upper-body AET	6.5–8.0	NR	62.0±5.9	↑ CRF (VO_{2peak}) ↔ Upper-extremity function (9HPT, handgrip power, Box and Block Test), aerobic endurance (6-minute wheelchair-test), fatigue (FSMC), depression (MDI), QoL (MSIS)
		5	4 weeks, standard MS rehabilitation	6.5-8.0	NR	55.2±8.2	
[30]	Pre-Post (IV)	8	18 sessions, electrical stimulation assisted cycling	6.5–8.5	NR	48.0±9.0	*↑ Thigh circumference ↑ Perceived muscle strength, leg circulation, spasticity and transfer ability

Table 1. (Continued)

[35]	Pre-Post (IV)	4	40 sessions, BWSTT	7.0–7.5	NR	47.0±5.3	↑ Muscle strength (MMT), walking speed (10-MWT), walking endurance (6MW), balance (BBS), spasticity (MAS), QoL (MSIS) ↔ EDSS (no formal statistics performed)
[32]	Pre-Post (IV)	6	12 weeks, BWSTT	6.0–8.0	11.5±6.6	48.2±9.3	*↑ QoL (MSQoL-54) ↓ Fatigue (MFIS), MSFC ↔ EDSS
[31]	Randomized clinical trial (IV)	6 6	12 weeks, TBRST 12 weeks, BWSTT	7.0 (mdn) 7.0 (mdn)	15.2±8.9 12.7±11.2	58.8±3.0 48.2±4.3	*↓ Fatigue (MFIS) ↑ QoL (MSQoL-54) ↔ EDSS or MSFC
[36]	Pre-Post (IV)	5	6 months, FES cycling	6.0–6.5	13	50 (mdn)	↑ Strength in muscles stimulated, MSFC scores, walking speed (T25FW), walking endurance (2MW), agility (TUG), QoL (SF-36) ↔ EDSS, spasticity (LLSMS), psychiatric functioning (SCL-90) Analysis of 120 cytokines, chemokines, and growth factors in CSF (*↓ MCP-1 only)
[37]	Pre-Post (IV)	31	12 weeks, aquatic exercise Women Men	 6.1±1.2 5.1±2.6	 NR NR	 50.4±10.8 52.7±9.1	*↑ Social functioning, fatigue domains of QoL (SF-36 & MSQLI), perceived social support (MSSS) ↔ Pain, sexual satisfaction, bladder control, bowel control, visual impairment, perceived deficits, mental health (domains of QoL)
[33]	Pre-Post (IV)	8 8	6 weeks, BWSTT Conventional therapy	4.5-6.5 4.5-6.5	17.1±12.0 18.6 ± 10.8	49.6±12 61.0±8.8	*↑ Walking speed (T25FW), walking endurance (6MW), gait ↑ Agility (TUG) ↓ Fatigue (FSS)

Table 1. (Continued)

[34]	Pre-Post (IV)	8	2 weeks, FES cycling	4.0–8.0	13.3±8.0	52.1±7.5	*↓ Acute spasticity (MAS) ↔ Strength, walking speed (T25FW), spasticity (MAS; post-intervention)
Emotional Well-being							
[56••, 57]	RCT (I)	19 21	8 weeks, Skype-delivered mindfulness intervention Wait-list control	6.8±1.6 6.2±1.4	16.24±10.1 12.57±8.6	53.42±8.3 50.9±9.9	*↓ Distress (GHQ-12), depression and anxiety (HADS), pain (non-specific numerical scale), QoL (MSIS psychological) ↓ Fatigue (FSS), QoL (MSIS physical), service use and costs (CSRI) ↑ QoL (ED-5D)
[58]	RCT (III)	8 8	6 individualized, one-to-one mindfulness sessions Waitlist control	NR NR	21.6±4.3 17.1±9.0	48.6±6.6 51.0±7.0	*↑ Timed single-leg balance task ↑ Symptom management (SRQ)
[59]	Pre-Post (IV)	39	10-week mindfulness-based cognitive therapy	3.9±1.7	11.2±7.9	48.2±8.5	*↓ Fatigue (CIS-20), depression and anxiety (HADS), cognitive symptoms (CFQ) *↑ Emotion-oriented coping (CISS), mindfulness (FFMQ-SF) ↓ Self-reported fatigue, negative emotions, and negative thoughts
Dietary Modification							
[75•]	Randomized clinical trial (III)	4 5	42-day, low-fat diet 42-day, low-fat diet with antioxidant supplementation	>6.5 >6.5	16±4.2 16±6.2	55.8±4.7 56.2±7.2	*↓ Serum CRP, 8-iso-PGF2α, IL-6 *↑ Catalase antioxidant activity ↓ Glutathione peroxidase ↑ SOD activity increase ↔ Glucose, total cholesterol, total lipids, protein (albumin & prealbumin), mineral concentrations, total antioxidant status

Table 1. (Continued)							
[76]	Pre-Post (IV)	10	Calorie restricted, modified Mediterranean diet with vitamin D, fish oil, lipoic acids, omega-3 polyunsaturated fatty acids, resveratrol, and multivitamin complex	4.2±0.7	NR	NR	↑ Serum PUFA concentration ↓ Serum MMP-9, fatigue (FSS), waist and hip circumference, and body weight ↔ Vitamin D levels, total cholesterol, triglycerides, fibrinogen, creatinine, depression (HAM-D), QoL (SF-36), EDSS
Combined							
[83]	Pre-Post (IV)	10	Modified Paleolithic diet + stretching and resistance exercises with NMES + meditation and massage	6.2±0.3	15.8±9.5	52.4±4.1	*↓ Fatigue (FSS)
[84-86]	Pre-Post (IV)	21	Modified Paleolithic diet + stretching and resistance exercises with NMES + meditation and massage	6.2±1.0	14.7±8.7	51.7±6.4	*↓ Fatigue (FSS) *↑ QoL (SF-36) *↑ Mood (BDI & BAI), cognition (DKEFS, FSIQ, WAIS) ↔ Gait (TUG, T25FW) and balance (BBS)

* Denotes significant change; ↑ = increase; ↓ = decrease, ↔ = no change.

Abbreviations: 2MW, 2-minute walk; **6MW**, 6-minute walk; **9HPT**, 9-hole peg test; **10-MWT**, 10-metre walk test; **T25FW**, timed 25-foot walk; **AET,** aerobic exercise training; **BAI,** Beck Anxiety Inventory; **BBS**, Berg Balance Scale; **BDI,** Beck Depression Inventory–II; **BDNF**, brain-derived neurotrophic factor ; **BWSTT**, body-weight support treadmill training; **CFQ**, Cognitive Failures Questionnaire; **CIS-20**, Checklist Individual Strength; **CISS**, Coping Inventory of Stressful Situations; **CRP**, C-reactive protein; **CSF**, cerebral spinal fluid; **CSRI**, Client Service Receipt Inventory; **DKEFS,** Delis-Kaplan Executive Function System; **EDSS,** Expanded Disability Status Scale; **EQ-5D,** EuroQoL; **FES**, Function Electrical Stimulation; **FFMQ-SF**, Five Facet Mindfulness Questionnaire, short form; **FSIQ**, Full-Scale IQ; **FSMC,** Fatigue Scale for Motor and Cognitive Functions; **FSS**, Fatigue Severity Scale-9; **GHQ-12**, General Health Questionnaire; **HADS**, Hospital Anxiety and Depression Scale; **HAM-D**, Hamilton Depression Rating Scale; **IDS,** Inventory of Depressive Symptoms; **LLSMS**, Lower Limb Spasticity Measurement System; **MAS**, Modified Ashworth Scale; **MCP-1** Monocyte Chemotactic Protein-1; **MDI**, Major Depression Inventory; **MFIS**, Modified Fatigue Impact Scale; **MMP-9**, metalloproteinase-9; **MMT**, Manual Muscle Test; **MSFC**, Multiple Sclerosis Functional Composite; **MSIS,**

Multiple Sclerosis Impact Scale; **MSQLI,** Multiple Sclerosis Quality of Life Inventory; **MSQoL-54**, Multiple Sclerosis Quality of Life-54; **MSSS**, Modified Social Support Survey; **NMES**, neuromuscular electrical stimulation; **QoL**, Quality of Life; **SCL-90**, Symptom Checklist; **SF-36**, 36-Item Short Form Survey; **SRQ,** Symptom Rating Questionnaire; **TBRST**, Total-Body Recumbent Stepper Training; **TUG**, Timed Up-and-Go test; **VLMT,** Verbal Learning and Memory Test, **VO_{2peak},** peak oxygen uptake; **WAIS,** Wechsler Adult Intelligence Scale.

Table 2. Feasibility metrics of wellness-based interventions in patients with progressive MS.

Reference	Drop-out (%)	Adherence (% of sessions attended)	Adverse Events
Exercise Training			
[27••, 28]	EX: 10.6% CON: 10%	NR	NR
[29•]	EX: 17% CON: 0%	EX: 96.0±5.0%	EX: No AEs reported during intervention. Hospitalization unrelated to intervention (n=1) CON: NR
[30]	12.5%	NR	NR
[35]	0%	NR	Reported as well-tolerated by all patients No increase in symptoms of fatigue
[32]	0%	97.7±3.7%	NR
[31]	BWSTT: 17% TBRST: 17%	BWSTT: 89.2±10.2% TBRST: 89.1±6.6%	BWSTT: Physical discomfort, minor bruising, joint pain, excessive fatigue TBRST: Physical discomfort, muscle pain, excessive fatigue
[36]	20%	NR	Increased spasticity (n=1), bowel incontinence (n=1; patient with irritable bowel syndrome), fall (n=1; unrelated to exercise training)
[37]	38.7% (19.4% prior to beginning trial)	25-49% (n=5) 50-74% (n=6) 75-100% (n=8)	Prior to trial: Exacerbation (n=2), extensive systemic infection (n=1) During trial: Exacerbation (n=2), attending the class made it difficult to complete daily tasks (n=2)
[33]	BWSTT: 11.1% CT: 11.1%	NR	NR
[34]	33%	NR	NR
Emotional Well-being			
[56••,57]	MIND: 0% CON: 5%	MIND: 50-100% CON: 85-100%	NR
Table 2. (Continued)			
[58]	MIND:12.5% CON: 0%	NR	NR

[59]	29%	71%	Fatigue (n=4), exacerbation (n=3)
Dietary Modification			
[75•]	DIET: 0% DIET + Antioxidant: 0%	NR	NR
[76]	DIET: 20%	NR	Reported as well-accepted by patients
Combined			
[83]	20%	Diet: >90% EX + NMES: >70%	Gastrointestinal distress, minor skin irritation following NMES (n=4) Headaches with high intensity of NMES (n=2)
[84-86]	10%	Diet: >94% EX + NMES: >75%	Gastrointestinal distress (n=9), irritability (n=1), fatigue (n=1), headache (n=1), and flushing with rash (n=1)

Abbreviations: BWSTT, body-weight support treadmill training; **CT**, conventional physiotherapy training; **CON**, control; **EX**, exercise; **MIND**, mindfulness; **NMES**, neuromuscular electrical stimulation; **NR**, not reported; **TBRST**, total-body recumbent stepper training.

Chapter 3

Characterizing Dietary Intake in Persons with Multiple Sclerosis

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Preface: This working paper included collaboration between myself, Amanda Gauthier, Dr. Isabelle Giroux, and my supervisor, Dr. Lara Pilutti. Amanda Gauthier and Dr. Isabelle Giroux were consulted with questions specific to dietary intake. This working paper was written by Myriam Venasse and reviewed by Dr. Lara Pilutti.

INTRODUCTION

Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system (CNS) that affects approximately 2.5 million people worldwide (1). As the disease progresses, damage occurs within different areas of the CNS, and this leads to a progressive increase in MS symptoms and impairments (2). These symptoms vary from one person to another, and include both physical (3–5) and psychological manifestations (6–16) that can lead to decreased engagement in activities of daily living and reduced quality of life (3,5). The lack of a cure for MS, and the inability for current disease-modifying therapies to prevent disability accumulation, warrants the examination of alternative approaches for disease management.

There has been recent interest from researchers and persons with MS in diet and how dietary approaches can be used to manage MS. Current research on the role of diet for persons with MS is inconclusive. As presented in a recent systematic review, most of this research has examined the role of diet in the risk of development, impact on progression, and potential for treatment of MS (17). The relationship between diet and disease activity and progression is supported by some evidence. Diets with higher intake of fruits, vegetables, unsaturated oils, vitamin B12 vitamins, antioxidants, various oil supplements, and omega 3 supplements, have been linked with decreased disease activity and disability in persons with MS (18–21). Polyunsaturated fatty acids (PUFA) supplements, antioxidants, fish oil, vitamin D, and a diet low in fat have also been linked with reduced relapse rates (22–26). Another study reported that using omega 3 and vitamin D_3 supplements together was linked with improvements in disability, inflammation, glycemic control, insulin levels, and lipid profiles in persons with MS (27). There are also other trials that have reported no link between intake of vitamins D and A and relapse rates in MS (28,29). The limited and conflicting research on diet and disease progression in persons with MS creates difficulty in recommending diets with therapeutic effects at this time. At present, there are no published MS-specific dietary guidelines or recommendations (30–32). Common recommendations made for persons with MS by researchers and health professionals include

balanced diets with low fat and high fiber intakes (30,31), and supplementation with vitamin D and omega 3-fatty acids (31,32).

Disease related factors, such as fatigue, pain, and difficulties with swallowing, may increase difficulties for persons with MS to complete tasks such as acquiring, preparing, and consuming healthy foods (33). A previous study reported that participants with mobility impairment faced barriers (i.e., mobility loss and fatigue) to engaging in healthy dietary behaviours (34). Some studies have examined the relationships between disability and dietary behaviours in persons with MS. One study focused on understanding the relationships between diet, quality of life, disability, and relapse rate (18). In this study, diets including a higher intake of fruits and vegetables, and a lower intake of dairy products and meat (i.e., a healthy diet) predicted lower disability levels and higher quality of life than an unhealthy diet (18). When comparing engagement in dietary behaviours between disability levels in this sample, persons with mild disability were more likely to engage in healthy dietary behaviours than persons with moderate or severe disability (18). As higher disability levels in MS are associated with worsening impairments (35), it might be expected that disability level could have an impact on dietary intake and engagement in dietary behaviours, such following specific diets, meal preparation, and food security. These relationships have yet to be comprehensively examined in persons with MS.

Studies have reported that over 40% of persons with MS follow specific diets (i.e., weight-loss, low calorie, low sugar, low-carbohydrate, gluten-free, and MS-specific such as the Wahls and Swank diets) (36). As previous research has identified some differences in dietary intake between persons with MS and controls, it is important to further examine dietary intake in these populations to gain better understanding of these differences. Not only do dietary intake and behaviours require further characterization in this population, but so do other factors that are related to dietary intake that are not often included in these studies (i.e., nutritional assessment, specific diets, food preparation, malnutrition, food security). Malnutrition (i.e., nutritional intake that is characterized by deficiencies, excesses, or imbalances) (37) has not been thoroughly examined

in persons with MS. One study reported that malnutrition may be more prevalent among persons with MS than among other chronic neurological diseases (i.e., headaches, vertigo, and lumbar discopathy) (38). Studies investigating malnutrition in MS are few, and additional studies should investigate whether malnutrition is more common among persons with MS than in the general population, and to determine whether there is potential for interventions targeting malnutrition in MS (38).

The objectives of this study were to: a) to characterize dietary intake in persons with MS based on disability status (i.e., with or without the use of assistive devices for ambulation) and with controls without MS; and b) and to examine dietary behaviours and other diet-related factors across groups. This work will provide new information on dietary intake in persons with MS with varying levels of disability, and will provide new information about the differences in dietary behaviours in persons with MS. This information can be used to guide future dietary interventions in persons with MS and to develop dietary recommendations and guidelines for this population.

METHODS

Study overview and design

This study used a cross-sectional design to characterize dietary intake in persons with MS with different disability levels, and compared to those without MS. We recruited a sample of 57 persons with MS with varying levels of disability categorized by the use of assistance in ambulation, as described below. A control sample of 57 persons without MS or other neurological conditions was recruited and matched to the MS sample based on age and sex. See Figure 1 for a flowchart of participant recruitment, exclusion, and completion.

Participant recruitment

Participants were recruited through information sheets or advertisements distributed through the North American Research Committee on Multiple Sclerosis (NARCOMS), the Multiple

Sclerosis Society of Canada's Research Portal, meetings and events associated with the Eastern Ontario Division of the MS Society of Canada, other online MS-based resources, local community outlets and online resources related to multiple sclerosis. The criteria for inclusion for all individuals were: (a) age between 18-65 years; (b) no history of any other neurological condition; and (c) willingness to complete a 3-day diet record and self-reported questionnaires. Additional criterion for participants with MS were a self-reported diagnosis of MS. The criterion for exclusion for all individuals was self-reported moderate (i.e., significantly interfering with function) or severe (little or no function possible) cognitive difficulty on the memory, calculation, and reasoning category of the self-reported EDSS scale (39). Controls were recruited through online and local community outlets. Recruited controls were matched to the MS sample based on age and sex (± 5 years).

Outcome measures

Demographics and health history. Participants completed a demographics questionnaire to describe individual and disease characteristics. From this questionnaire, self-reported height and weight were used to calculate body mass index (BMI), as weight in kilograms divided by height in meters squared. The categorization of BMI was according to standard values: underweight, BMI<18.5kg/m^2; normal weight, BMI=18.5-24.9kg/m^2; overweight, BMI=25.0-29.9kg/m^2; and obese, BMI≥30.0kg/m^2 (40). The Self-Administered Comorbidities Questionnaire (41) was used to record participant health history. Comorbidities were collected for descriptive purposes and to gain a better understanding of medication and supplement intake. Physical activity was measured using the Godin Leisure-Time Exercise Questionnaire (GLTEQ) (42). These data were collected to determine differences in physical activity levels across groups and for use in the calculation of dietary intake variables.

Neurological disability status. The Patient Determined Disease Steps (PDDS) scale was used to assess neurological disability level in participants with MS (43), and to categorize their disability as without the use of assistive devices (i.e., mild disability, scores from 0-3.0), and with use of

assistance for ambulation (i.e., moderate-to-severe disability, scores from 4.0-8.0).

Dietary intake. Dietary intake was assessed using a 3-day food intake record. Participants received detailed information for how to record their dietary intake using a spreadsheet. They were instructed to use measuring cups, spoons, or make estimates using their own hand to measure everything that they ate and drank over a 3-day period, including supplements (i.e., vitamins, minerals, and other dietary supplements) and medications. Participants were instructed to complete the food intake record within 7 days, and for one weekend day and two week days. ESHA The Food Processor (Salem, Oregon) was used to enter and analyze dietary intake data. These data were examined both with and without the intake of supplements. Specific outcomes determined from the food intake records (i.e., total caloric intake, macronutrient and micronutrient intake, vitamins and minerals) were used to determine whether participants met their DRI for all nutrients using current Canadian Dietary Reference Intake recommendations (44). The current Dietary Reference Intakes (DRIs) include a group of dietary recommendations, such as the Recommended Dietary Allowances (RDA), Estimated Energy Requirements (EER), and Adequate Intakes (AI) (44) There are currently no recommended RDI values specific to persons with MS, therefore energy intake was calculated EER (44). Percentages around 100% would indicate that participants were consuming the recommended amount of these nutrients. Percentages below 100% would indicate that participants consumed a lower amount of a nutrient than what is recommended, and percentages above 100% would indicate that participants consumed a higher amount of a nutrient than what is recommended. These percentages were calculated by ESHA The Food Processor using the age, sex, height, weight, and activity level for each participant, based on their individual dietary reference intakes (45).

Dietary behaviours scale. Participants completed a 5-item dietary behaviours scale that was used to assess global dietary behaviours across groups (46). Participants indicated whether they rarely, sometimes, or often, engaged in these behaviours (i.e., making good food choices, eating five servings of fruits and vegetables per day, limiting fat intake, reading labels, and eating regularly).

Scores range from 0-10, with higher scores indicating healthier dietary behaviours.

Dietary self-efficacy. Dietary self-efficacy was measured using a combined 15-items from two separate dietary self-efficacy scales. A 5-item scale assessing levels of confidence (from 1=not at all to 10=completely) for engaging in specific dietary behaviours (i.e., eating a well-balanced diet, following a diet recommended by your doctor, selecting foods that will help you maintain weight, selecting appropriate vitamins and supplements, and identifying nutrients by reading food labels). This scale has been used in one study with participants with physical disabilities including MS (46), and was developed in studies of chronic diseases (47,48). Given the limited number of items in the latter scale, dietary self-efficacy was also captured using 10 of the 16 items from the Cardiac Diet Self-Efficacy Scale (CDSES), a more general measure of dietary self-efficacy assessing levels of confidence (from 1=very little to 5=quite a lot) for engaging in healthy dietary behaviours (49). This scale has not been used in studies with participants with MS.

Other dietary information. Participants were asked a series of questions about dietary recommendations, nutritional assessment, malnutrition, meal preparation, and food security. Participants were asked who usually prepared meals at home (e.g., I cook for myself, someone else in my home cooks for me, I have a service that delivers prepared food to me, other). Participants were asked if they had ever undergone a nutritional assessment (i.e., in-person evaluation of prospective food records or retrospective food frequency questionnaires or diet history conducted by a Registered Dietician or another health professional) from a registered dietician (50). Participants were asked if they had ever received a specific nutritional diagnosis, and if so, to list the specific diagnosis (e.g., deficiency or surplus of vitamins, minerals, or calories, food intolerance). For characterization purposes, participants were asked whether or not they currently followed a specific diet (e.g., Paleo, Swank). If they followed a specific diet, they were asked what resulted in this decision (i.e., recommendation from a Registered Dietician or another health professional, recommended by family or friends, etc.). Further, they were asked two questions from the Canadian Nutrition Screening Tool (CNST) related to change in weight status

and eating patterns over the last 6 months as potential indicators of malnutrition (51). An answer of “yes” to both of these questions would indicate nutrition risk, and the need for further patient assessment for malnutrition. One question examining food security, taken from the Canadian Community Health Survey was included (52). This question examined participants’ level of food security over the last 12 months, and asked participants to indicate whether they: 1) always had enough of the kinds of food they wanted to eat; 2) always had enough to eat, but not always the kinds of foods they wanted; 3) sometimes did not have enough to eat; or 4) often did not have enough to eat.

Procedures

Interested individuals contacted the laboratory to receive further information regarding study participation. Participant screening was conducted over the telephone using a checklist of criteria. Eligible participants were mailed or emailed an informed consent form to review and sign, along with a study packet. The study packet included detailed instructions to complete the food intake record, and all self-report questionnaires. A member of the research team contacted participants approximately 3-5 days after the materials were distributed to ensure that the packet was received and to review the consent form and instructions. Participants were asked to refrain from completing the testing packet until all instructions had been reviewed with a member of the research team. Participants were then asked to complete the dietary record and other materials within one week. Participants who chose to receive the materials by mail were provided with two pre-addressed, pre-stamped envelopes to return the consent form and questionnaires in separate envelopes to the research team. Participants who chose to complete the materials online received a dedicated study link to complete the questionnaires through Google Forms. These participants were asked to return their signed consent form by email using a dedicated laboratory email. Once the materials were received by the researchers, data were checked for completeness and missing responses were verified with the participant via phone or email. Participants received a $15 gift

card as well as an informative handout containing resources for additional information on diet and nutrition.

Data analysis

Data were analyzed using IBM SPSS Statistics Version 25.0 (Armonk, NY). Data were first examined for normality violations, errors, and outliers. Only participants who completed both the diet record and questionnaire packet were included in final data analyses. Differences in dietary patterns by group (i.e., control, MS without assistive device, MS with assistive device) were examined using a one-way analysis of variance, that was controlled for physical activity across the groups (i.e., ANCOVA). Differences across groups were decomposed using Bonferroni *post-hoc* analyses. Differences across groups for categorical variables were examined using chi-square tests. Differences between the MS groups only were examined using *t*-tests. Values are presented within the text as mean (SD), unless otherwise noted.

RESULTS

Participants

Of the 201 individuals who contacted the research team, 103 were persons with MS and 98 were healthy controls. Of these 201 individuals, 24 persons with MS and 24 matched controls could not be reached for screening. The remaining 79 persons with MS and 74 healthy controls were screened for eligibility. Two persons with MS and 13 controls did not meet inclusion criteria, and eleven persons with MS and 3 controls were not interested in participating after hearing more about the study. The remaining 66 persons with MS and 58 controls were eligible and enrolled to the study. Of these individuals, 4 persons with MS withdrew following enrollment, 5 persons with MS and 1 control partially completed the study (e.g., diet record or questionnaire packet only), and 57 persons with MS and 57 controls fully completed the study (see Figure 3).

Demographic and clinical characteristics for each group (i.e., controls, mild disability, moderate-to-severe disability) are presented in Table 1. There were no significant differences in age and sex (approximately 80% female) across groups. There were differences in employment status across groups (p<.001). There were also differences in the areas that participants lived across groups (p<.001). The control group and the mild MS group were classified as overweight, while the moderate-to-severe MS group was classified as normal weight. There were significant differences in physical activity between groups (F [2,110]=7.0, p=.001, ηp^2=.113), and post-hoc comparisons revealed significant differences between persons with MS in the moderate-to-severe disability group and the mild disability MS group (p=.012) and the control group (p=.001). As expected, there were significant differences in disability scores between the two MS groups t (56) =.13, p<.001. The average disease duration for MS groups were 11.7 and 16.4 years, respectively, and this was not statistically different between groups. In the mild disability MS group, 94.3% of the group had relapsing-remitting MS (RRMS), and the remaining were not sure of their MS type. In the moderate-to-severe disability MS group, 22.7% had RRMS, and 77.3% had progressive types of MS. There were significantly more persons with RRMS in the mild disability group (χ2 (3)=38.7, p < .001) than the moderate-to-severe disability group.

Dietary intake

When examining daily dietary intake including supplements (Table 2), there were differences across groups in vitamin D intake (F [2,109]=3.3, p=.04, ηp^2=.058), vitamin B12 intake (F [2,109]=4.9, p=.01, ηp^2=.082), vitamin C (F [2,109]=8.5, p<.001, ηp^2=.135), and folate (F [2,109]=4.2, p=.03, ηp^2=.072), and post-hoc comparisons revealed significant differences between participants with MS with mild disability and controls (all p<.05). When supplements were removed from the dietary intake (Table 3), there were significant differences across groups in vitamin C intake (F [2,109]=4.1, p=.02, ηp^2=.070), and post-hoc comparisons revealed significant differences between participants with MS with mild disability and controls (p=.02). There were also

significant differences in manganese intake across groups (F [2,109]=3.2, p=.04, ηp^2=.057), and post-hoc comparisons revealed significant differences between participants with MS with moderate-to-severe disability and controls (p=.04). When examining whether the control and MS groups were meeting RDI, it was observed that most nutrients were either consumed in quantities below (e.g., AI for omega 3 and omega 6, RDA for molybdenum) or above (e.g., RDA for vitamin B12 and vitamin C, AI for biotin) DRI. There were no other differences in dietary intake with or without supplements across groups.

Dietary behaviours, self-efficacy and other dietary information

Self-reported dietary behaviours, self-efficacy and other dietary information are presented in Table 4. Dietary behaviours scores were similar across the three groups (m=7.6, 7.8, and 8.0), respectively, and so were dietary self-efficacy scores (m=113.8, 114.3, and 121.8). There were no differences in the number of persons who followed specific diets between groups (p=.55). The most common diets in the control group were gluten free (n=1), paleo (n=1), and others (n=7). The most common diets in the MS groups were the Wahls Diet (n=4), gluten free (n=3), paleo (n=2), and Swank (n=2). In terms of dietary recommendations, most persons across groups reported obtaining these from 'other sources' (e.g., family, friends, online; 10.8%, 17.4%, 13.5%). Fewer participants reported receiving dietary recommendations from a Registered Dietician or health practitioner (3.5%, 11.5%, 0%). There were differences, although not statistically significant, in the number of persons that reported receiving a nutritional assessment across the groups (10.5%, 17.1%, 31.8%), suggesting that persons with MS with higher disability may be more likely to have a nutritional assessment. There was a significant difference across groups in self-reported weight decrease of ≥5% of body weight or greater over the last 6 months ($\chi 2$ (3) = 7.1, p=.03). This difference in self-reported weight decreases was observed between persons with mild MS and moderate-to-severe MS ($\chi 2$ (3) 4.3, p=.01) and between persons with mild MS and matched controls ($\chi 2$ (3) = 7.2, p=.002). There were no other differences in self-reported dietary behaviours

or information across groups. Over half of participants in each group reported that they prepared meals for themselves (78.9%, 80.0%, 59.1%), a smaller proportion reported that someone else in the home cooked for them (12.3%, 8.6%, 31.8%), and fewer reported that there were shared cooking duties in the home (8.8%, 11.4%, 9.1%). When examining food security, over 80% of participants within each group reported that they 'always had enough of the kinds of foods that they wanted to eat' (82.5%, 91.4%, 81.8%), and the remaining participants reported that they 'always had enough to eat, but not always the kinds of foods that were wanted' (17.5%, 8.6%, 18.2%).

Comorbidities, medications and supplements

The presence of comorbid health conditions, and medication and supplement intake are presented in Table 5. The overall prevalence of comorbidities was 54% in the control group and 51% in the MS group. Back pain (n=28, 24.5%), depression (n=23, 20.2%), and high blood pressure (n=18, 15.8%) were the most commonly reported comorbidities among all groups. Overall, 22% of controls and 45% of persons with MS reported taking any medication. The most commonly used medications in the three groups were those for cardiovascular and metabolic indications. In the MS groups, 22% of the sample reported taking disease-modifying therapies (e.g., Tecfidera, Gilenga, Aubagio). In this sample, 40.3% of controls and 54.3% of persons with MS reported using dietary supplements. When examining supplement use, vitamin B12, vitamin B complex, vitamin C, vitamin D, and multivitamins were the most commonly used across the groups. For minerals, magnesium and calcium were the most commonly used minerals across the groups. When examining other supplement use, probiotics and enzymes were the most commonly taken across the groups.

Discussion

The objectives of this study were to characterize dietary intake in persons with MS based on disability status, and with a matched control sample without a neurological disorder. We further aimed to characterize dietary behaviours and other factors affecting dietary intake across groups. Our results indicate that there were no differences in dietary intake and behaviours between persons with MS based on disability status, and few differences emerged compared to persons without MS. Differences in dietary intake across groups were seen in vitamin intake, and these differences were primarily accounted for by supplement intake by persons with MS. Collectively, these results suggest that dietary intake in persons with MS is similar to that of persons without MS, and that persons with MS are supplementing more than persons without MS.

In the present study, there were no differences by MS disability group in estimated energy requirements, caloric intake, and macronutrient intake. However, other research examining the relationships between dietary intake (through a Dietary Habits Questionnaire) and disability in persons with MS have observed some differences by disability level. This study observed that a healthier diet (i.e., greater vegetable and fruit intake, and lower dairy and meat intake) predicted lower levels of disability and better quality of life (18). In that same study, persons in the mild disability group were more likely to engage in healthier dietary behaviours than those in the moderate or severe disability groups (18). Our results are similar to another study reporting on the diet quality (Dietary Screener Questionnaire) of persons with MS where overall diet composition did not vary by disease course or disease duration, and there were no differences between the diet quality scores of persons with MS and age-matched controls without MS (36). It is possible that the differences between studies are due to the different measures of dietary intake (i.e., food intake record, dietary screener questionnaire, and dietary habits questionnaire) that were used in each study. This could further be attributed to differences in the disability level of the samples. In our study, there were fewer persons with MS in the moderate-to-severe group and the sample did not include many persons with MS at the high end of the disability spectrum (i.e., nonambulatory).

A sample including more individuals with higher disability levels may be required to observe differences in dietary intake and behaviours based disability status.

There were no differences in dietary intake between persons with MS with mild disability and moderate-to-severe disability. Few differences emerged in dietary intake between persons with MS and controls without MS. Differences were primarily observed for intake of certain vitamins (D, B12, C and folate). Other studies comparing dietary intake in persons with and without MS reported that the intake of fruits, vegetables, legumes, fibre, and whole grains by persons with MS were comparable to age-matched controls (36). This same study also reported that persons with MS consumed less sugar, dairy, and calcium, and that they consumed more red and processed meats when compared to the control sample (36). Studies investigating dietary intake have been limited, and have used a variety of measures such as 24-hour recalls, food frequency questionnaires, diet quality scores, and food intake records to examine dietary intake in persons with MS (46,53,54). This can lead to some difficulties when making comparison across studies. To our knowledge, the present study is the only study characterizing dietary intake prospectively through a food intake record, which provided detailed information on the nutrient intake of persons with MS and matched controls.

When examining DRI for all nutrients in the present study, the intake of most nutrients was either inadequate or greater than the recommended amounts. The results from the present study are similar to a previous study examining eating patterns of women with MS that reported participants were either consuming amounts greater than or lesser than recommended (55). Specifically, the intake of carbohydrates, fiber, vitamin E, calcium, and zinc, were inadequate when compared to those calculated by software (i.e., The Food Processor) (55). In that same study, the intake of saturated fat, protein, vitamin A, vitamin C, folate and iron were greater than the RDA (55). In the present study, the intake of carbohydrates and calcium were below RDA, and the intake of fiber, omega 3, and omega 6 were below AI. The intake of protein, vitamin D, vitamin B12, vitamin C, and iron was above RDA for all three groups. The intake of sodium, biotin, and

manganese were above AI for all three groups. The intake of fat and saturated fat were also above DRI for all three groups. Our findings are contradictory to studies that have been conducted in elderly and other disabled populations, which have found that nutrient intakes are often not met (56,57), as some nutrient intakes surpassed recommendations in this sample. It is also important to note that it is challenging to determine whether persons with MS are meeting DRIs, as there are currently no MS-specific recommendation for dietary intake, and it is possible that dietary needs may be different in persons with MS compared to those without MS. Therefore, encouraging persons with MS to consult a Registered Dietician or other healthcare providers is important to ensure their individual needs are assessed (58).

In this study, 54.3% of persons with MS and 40.3% of the control group reported using dietary supplements. Both of these values are lower than studies that have examined dietary supplement use in persons with MS (17,59,60) and in the general population (52,61). Vitamin D was one of the most commonly used supplements in this sample, particularly in the MS groups, which explains the values exceeding RDA for this vitamin in persons with MS. Vitamin D supplementation is commonly recommended in the general population (52), and is one of the only vitamins with evidence to recommend supplementation for persons with MS (32). For persons with MS, oral vitamin D supplements are strongly recommended, with doses ranging between 800-2000 IU per day (62). It is possible that participants were also supplementing with vitamin D for osteoporosis, although only 6 participants with MS reported this comorbidity and this was not different than the control sample. The intake of vitamin B12 was also above RDA for all three groups, and was particularly high among persons with MS. Research examining B12 in MS has reported that B12 deficiency can lead to demyelination and axonal injury (63). In another study conducted with a MS mouse model, lower levels of disability and demyelination were observed in mice who received B12 supplements and Interferon-β, which is commonly used in therapies for demyelinating diseases (64).

The present study also observed that vitamin C intake surpassed RDA for all three groups, with and without supplements. Vitamin C consumption was higher in the MS groups than the control group. These results conflict with previous research on vitamin C intake in persons with MS and controls (n = 74; EDSS < 4.5), where there were no differences between MS and control groups, and where the intake of vitamin C was below RDA (65). Vitamin C is a widely used dietary supplement that acts as an antioxidant and has many roles within the CNS, such as in the formation of the myelin sheath around neurons (66). The possible role of vitamin C in MS course still has to be explored (66); however, it's potential positive effects on the disease may explain the higher consumption of vitamin C by persons with MS when compared to controls. This same study also examined folate intake in persons with MS and controls, and similar to our study, found no significant differences between persons with MS and the control group in dietary intake (i.e., without supplements). In the present study, the difference between groups in folate intake was only observed for dietary intake including supplements.

When examining mineral supplement intake, magnesium and calcium were the two most common in all three groups, yet RDA for both of these minerals was below recommended amounts. Magnesium deficiency due to malnutrition or due to an increased demand because of the disease may lead to worsening of certain symptoms in MS, such as fatigue (67). Calcium supplements may have been taken in combination with vitamin D as a preventative method against osteoporosis, which is a common comorbidity among persons with MS (31). Probiotics and digestive enzymes were also commonly used in this sample. This might indicate that persons with MS are experiencing digestive issues, or that they may be taking certain medications that may lead to digestive issues. A randomized controlled trial of probiotics in people with MS reported positive effects on disability, mood, and markers of inflammation and metabolism (27).

There were no significant differences in self-reported dietary behaviours and self-efficacy across groups. Dietary self-efficacy was overall high in all groups, which identifies that dietary self-efficacy could be a great target for future interventions in persons with MS and the general

population as well. Previous research using these scales with a persons with MS have not included subgroup comparisons or control samples without MS (46–49). There were no relationships between the dietary behaviours scale and macronutrient intake, and a few relationships between this scale and vitamin and mineral intake. The present study observed no significant differences across groups in the specific diets that were followed by participants, and there were few participants who reported following a specific diet. A recent study of dietary characteristics in a large MS sample observed that approximately 45% of the sample reported having tried following a diet (i.e. weight loss-plan, low-calorie, low-carbohydrate, low-sugar), and very few people reported following MS-specific diets (i.e., Wahls, Swank) (36). When examining the number of persons who had received nutritional assessments across groups, there was no significant difference, although there were more people in the moderate-to-severe MS disability who had received a nutritional assessment than in the other two groups. To our knowledge, there are no other studies that have reported the number of persons with MS having received a nutritional assessment.

The only significant difference observed when examining other diet information across groups was in self-reported weight decreases of ≥5% of body weight over the last 6 months. Based on their answers to questions regarding weight and eating pattern changes, there were no individuals whose answers would indicate that they are at nutrition risk, and that they should be further assessed for malnutrition. Persons with milk MS self-reported more weight decreases of ≥5% of body weight than the other groups, and it is possible that this is happening because these individuals might be improving their dietary and physical activity behaviours following their MS diagnosis. A study examining dietary changes in behaviours in a sample of individuals who received a first clinical diagnosis of CNS demyelination reported that 38% of their sample made at least one dietary change within the first year following their diagnosis, and that most of these changes were toward improving the quality of their diet (68). Unfortunately, with the data that was collected for the present study, it is not possible to determine if the decreases in weight are due

to dietary changes, or to other factors. Nonetheless, future research should continue to monitor for malnutrition in MS, as one previous study reported there is a higher prevalence of malnutrition in the MS population than in other chronic neurological diseases (38). Previous studies examining nutritional behaviours have reported that persons with MS who use assistive devices had difficulty with preparing meals, and that they often relied on family members to do grocery shopping and meal preparation for them. In the present study, there were no significant differences between the mild disability and moderate-to-severe disability groups. However, there were more persons with MS with moderate-to-severe disability who reported that someone else in the home was completing meal preparation. The present study observed no significant differences in food security across groups. To our knowledge, there are no other studies that have examined food security in people with MS. A recent scoping review examining disability, food access, and disability reported that disability is often associated with high levels of food insecurity across many populations and geographic settings (69). As previous research examining dietary information such as nutritional assessment, meal preparation, and food security in persons with MS is limited, it is difficult to compare our results to those of previous studies. Therefore, future research examining dietary intake in persons with MS should include additional questions examining other dietary behaviours such as those listed above that may influence dietary intake and health in this population.

This study is not without limitations. The data were self-reported, however, most scales used in this project were validated against clinically-administered scales and also show good psychometric properties. Another limitation is that dietary intake can be challenging to assess for multiple reasons. For example, there is the possibility that participants may have modified their intake, or reported a smaller or larger quantity of certain foods during the monitoring period, as has been reported in other studies (70). In an attempt to limit this effect, the food intake record was explained to participants in detail and they were instructed to report their dietary intake as honestly and accurately as possible. Participants were asked to complete the food intake record

for two weekdays and one weekend day, maintaining their usual intake, and avoiding days with irregular eating patterns (e.g., holidays). Food intake records can have high participant and researcher burden (70). However, examining dietary intake through a 3-day food intake record allowed us to collect quantitative dietary information without requiring subject recall. Another limitation to address is that persons with MS and controls with little interest in dietary behaviours may have been less likely to reach out to us and to participate in this study. Therefore, the sample might not be representative of the MS population overall. In an effort to limit this effect, recruitment materials were distributed as broadly as possible, and the study was made available through different modes of completion. Additionally, dietary intake data were collected over one three-day period, making it impossible to examine dietary habits over time. It will be important for future studies to investigate if disability level or other factors may be related to dietary intake over time. Lastly, while participants who were following a specific diet were asked why they did so, they were not asked the same question about their dietary supplement intake. Understanding where persons with MS received the recommendation to take these dietary supplements would have helped clarify differences between groups.

In summary, there were few differences in dietary intake based on MS disability levels, and compared to persons without MS. Significant differences were seen specifically in vitamin intake, and these differences were accounted for by supplement intake. There were no significant differences in dietary intake and behaviours based on disability status, and no significant differences in other dietary behaviours, with the exception of self-reported weight changes. To our knowledge, no previous study has examined differences in dietary intake by disability status in persons MS, with a control group for comparison, using a prospective food intake record. Additional studies with larger samples are necessary to further our understanding of differences in dietary intake and behaviours based on clinical disease characteristics among persons with MS.

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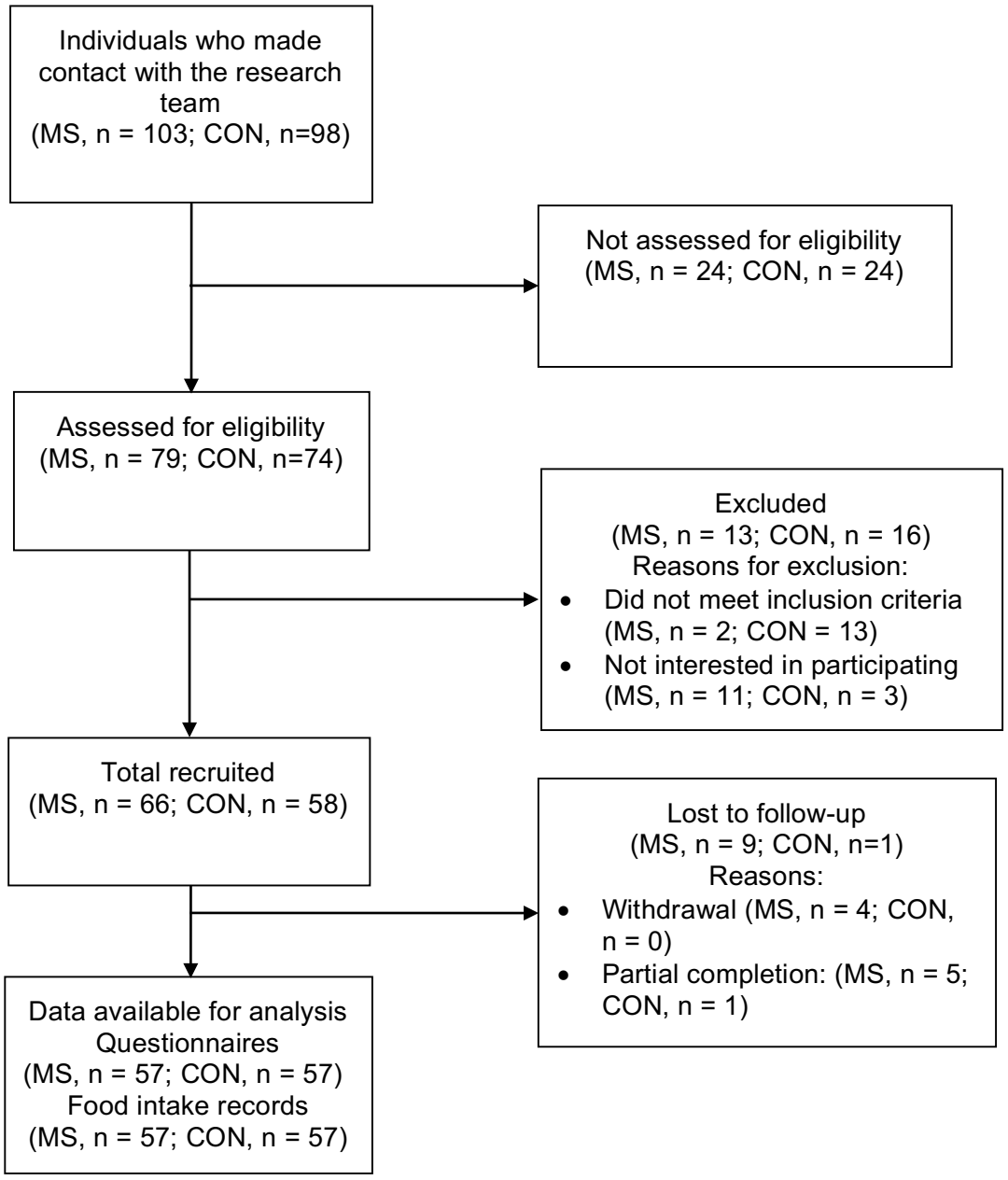
Chapter 3

Figures and Tables

Figure 1. Flowchart of participant recruitment, exclusion, and completion.



MS: multiple sclerosis; CON: control group.

Table 1. Demographic and clinical characteristics for all participants. Values are reported as means and SD unless specified otherwise.

Variable	Control (n=57)	Mild MS (n=35)	Moderate-Severe MS (n=22)	F/χ2/t value	*p*-value
Age (years)	48.4 (11.1)	46.5 (10.6)	50.3 (8.1)	.93	.39
Sex (% female)	82.5	80.0	81.8	.11	.89
Height (cm)	166.6 (8.4)	167.7 (7.9)	166.6 (9.1)	.23	.79
Weight (kg)	74.6 (17.8)	74.3 (21.1)	67.8 (15.0)	1.0	.35
BMI (kg/m^2)	26.8 (5.7)	26.3 (7.2)	24.5 (5.7)	1.0	.37
Education (n, %)				15.4	.05
Partial high school	0	3 (8.6)	0		
High school	7 (12.3)	4 (11.4)	3 (13.6)		
College	9 (15.8)	8 (22.9)	9 (40..9)		
Bachelor's degree	27 (47.4)	12 (34.3)	9 (40.9)		
Master's or higher	14 (24.6)	8 (22.9)	1 (4.5)		
Employment (n, %)				62.5	**<.001**
Employed	50 (87.7)	22 (62.9)	3 (13.6)		
Unemployed	2 (3.5)	2 (5.7)	2 (9.1)		
Retired	4 (7.0)	6 (17.1)	0		
Unable to work due to illness or disability	1 (1.8)	5 (14.3)	17 (77.3)		
Income (n, %)				13.0	.22
Less than $15,000	1 (1.8)	2 (5.7)	1 (4.5)		
$15,001-$30,000	0	1 (2.9)	1 (4.5)		
$30,001-$50,000	5 (8.8)	1 (2.9)	5 (22.7)		
$50,001-$100,000	15 (26.3)	12 (34.3)	6 (27.3)		

Table 1. (Continued)					
Over $100,000	28 (49.1)	12 (34.3)	5 (22.7)		
Prefer not to answer	8 (14.0)	7 (20.0)	4 (18.2)		
Area lived in (n, %)				19.2	**.001**
Urban	18 (31.6)	14 (40.0)	8 (36.4)		
Suburban	37 (64.9)	10 (28.6)	8 (36.4)		
Rural	2 (3.5)	11 (31.4)	6 (27.3)		
Physical activity	42.5 (29.8)	38.8 (32.4)	15.9 (18.8)	7.0	**.001**
PDDS (mdn, IQR)	-	1.0 (2.0)	6.0 (2.0)	.13	**<.001**
MS Type				38.7	**<.001**
Relapsing	-	94.3	22.7	-	-
Progressive	-	0	77.3	-	-
Unknown	-	5.7	0	-	-
Disease duration (years)	-	11.7 (9.2)	16.4 (9.7)	2.7	.10

MS: multiple sclerosis; cm: centimetre; kg: kilogram; m: metre; BMI: body mass index; PDDS: Patient Determined Disease Steps Scale; mdn: median; IQR: inter quartile range.

Table 2. Average dietary intake per group with supplements expressed as a percent of the dietary reference intake recommendations.

Variable (% recommendation)	Controls (n=57)	Mild MS (n=35)	Moderate-Severe MS (n=22)	F-value	*p*-value	ηp^2
Total energy (kcal)	85.2 (25.4)	89.1 (25.7)	86.5 (22.7)	.26	.77	.005
Protein (g, RDA)	140.0 (49.3)	147.2 (58.9)	155.0 (53.8)	.67	.51	.012
Fat (g)	113.8 (39.9)	115.9 (43.5)	121.9 (40.6)	.27	.76	.005
Saturated fat (g)	121.6 (53.7)	109.8 (53.7)	117.1 (46.2)	.59	.56	.011
Carbohydrates (g, RDA)	71.1 (26.7)	75.7 (29.9)	70.5 (18.1)	.52	.59	.010
Fiber (g, AI)	74.1 (35.1)	80.2 (39.3)	78.3 (28.5)	.48	.62	.009
Cholesterol (mg)	93.3 (38.3)	93.8 (62.8)	83.5 (47.3)	.32	.72	.006
Vitamin D (mcg, RDA)[a]	55.2 (135.5)	181.9 (363.4)	178.3 (267.1)	3.3	.04	.058
Omega 3 (g, AI)	36.5 (28.0)	60.6 (60.5)	56.5 (78.7)	2.6	.07	.046
Omega 6 (g, AI)	30.1 (17.1)	33.4 (24.6)	28.7 (13.8)	.46	.63	.008
Vitamin A (mcg. RDA)	91.5 (85.3)	98.6 (72.1)	145.3 (192.8)	1.7	.18	.030
Vitamin B12 (mcg, RDA)[a]	189.1 (207.6)	690.2 (1180.0)	652.7 (1058.5)	4.9	**.01**	.082
Vitamin C (mg, RDA)[a]	184.12 (201.2)	609.4 (711.1)	433.2 (558.4)	8.5	**<.001**	.135
Sodium (mg, AI)	155.1 (87.9)	143.8 (59.2)	174.5 (134.3)	.70	.49	.013
Phosphorous (mg, RDA)	111.2 (57.8)	93.7 (55.4)	77.6 (45.3)	2.8	.06	.051
Calcium (mg, RDA)	80.9 (40.3)	99.0 (67.5)	79.5 (39.2)	1.6	.20	.029
Folate (mcg, RDA)[a]	66.4 (110.5)	106.4 (110.5)	61.2 (38.2)	4.2	**.03**	.072
Iron (mg, RDA)	123.3 (73.0)	157.7 (146.6)	143.2 (85.2)	1.2	.29	.022
Biotin (mcg, AI)	197.7 (705.5)	355.7 (807.7)	777.0 (1687.6)	2.3	.10	.041
Magnesium (mg, RDA)	71.2 (34.8)	113.6 (126.9)	77.9 (71.7)	3.1	.05	.053
Manganese (mg, AI)	145.5 (99.4)	141.3 (105.1)	112.2 (60.4)	.85	.43	.015
Molybdenum (mcg, RDA)	45.5 (57.1)	44.8 (69.7)	37.3 (49.0)	.14	.86	.003
Zinc (mg, RDA)	87.5 (59.2)	115.0 (133.6)	94.6 (73.7)	.99	.37	.018
Water (g, AI)	62.3 (40.9)	60.1 (40.2)	52.3 (33.5)	.44	.65	.008

[a]Indicates a significant difference between controls and Mild MS. MS: multiple sclerosis; kcal: kilocalorie; RDA: recommended daily allowance; g: gram; AI: adequate intake; mg: milligram; mcg: microgram.

Table 3. Average dietary intake per group without supplements expressed as a percent of the dietary reference intake recommendations.

Variable (% recommendation)	Controls (n=57)	Mild MS (n=35)	Moderate-Severe MS (n=22)	F-value	*p*-value	ηp^2
Total energy (kcal)	85.2 (25.4)	89.1 (25.7)	86.5 (22.7)	.18	.83	.003
Protein (g, RDA)	140.0 (49.3)	147.2 (58.9)	155.0 (53.8)	.63	.53	.011
Fat (g)	113.8 (39.9)	115.9 (43.5)	121.9 (40.6)	.27	.76	.005
Saturated fat (g)	121.5 (49.6)	108.8 (53.5)	119.1 (46.4)	.66	.52	.012
Carbohydrates (g, RDA)	71.1 (26.7)	75.7 (29.9)	70.5 (18.1)	.40	.67	.007
Fiber (g, AI)	74.1 (35.1)	80.2 (39.3)	78.3 (28.5)	.32	.73	.006
Cholesterol (mg)	93.3 (38.3)	93.8 (62.8)	83.5 (47.3)	.32	.72	.006
Vitamin D (mcg, RDA)	14.0 (15.8)	14.5 (15.1)	16.8 (13.3)	.23	.79	.004
Omega 3 (g, AI)	34.7 (27.2)	48.5 (53.8)	51.9 (73.7)	1.3	.26	.024
Omega 6 (g, AI)	30.1 (17.1)	33.4 (24.6)	28.6 (13.8)	.48	.62	.009
Vitamin A (mcg. RDA)	91.1 (85.7)	90.0 (67.4)	132.7 (148.6)	1.5	.23	.027
Vitamin B12 (mcg, RDA)	176.8 (389.1)	128.7 (115.9)	138.9 (295.6)	.28	.75	.006
Vitamin C (mg, RDA)[a]	145.8 (83.9)	379.2 (639.8)	376.2 (506.5)	4.1	**.02**	.070
Sodium (mg, AI)	154.9 (87.9)	143.0 (59.4)	174.6 (134.3)	.74	.48	.013
Phosphorous (mg, RDA)	111.2 (57.8)	91.2 (54.5)	77.7 (45.3)	3.0	.05	.053
Calcium (mg, RDA)	76.9 (38.6)	75.5 (35.1)	76.3 (35.5)	.02	.98	.000
Folate (mcg, RDA)	61.6 (37.2)	70.3 (41.4)	55.7 (37.2)	.99	.37	.018
Iron (mg, RDA)	120.2 (73.4)	122.4 (71.7)	124.6 (65.3)	.03	.97	.001
Biotin (mcg, AI)	60.4 (76.6)	43.8 (37.1)	39.9 (29.1)	1.3	.28	.023
Magnesium (mg, RDA)	65.7 (66.5)	62.6 (40.2)	55.5 (22.9)	.64	.53	.012
Manganese (mg, AI)[b]	137.3 (97.1)	102.9 (57.4)	91.1 (50.9)	3.2	**.04**	.057
Molybdenum (mcg, RDA)	40.3 (47.3)	22.7 (24.8)	22.5 (15.9)	3.0	.05	.053
Zinc (mg, RDA)	78.7 (41.9)	63.2 (37.1)	58.1 (38.2)	2.6	.08	.046
Water (g, AI)	62.3 (40.9)	60.1 (40.3)	52.3 (33.5)	.44	.65	.008

[a]Indicates a significant difference between controls and Mild MS; [b]Indicates a significant difference between controls and Moderate-Severe MS. Multiple sclerosis: MS; kcal: kilocalorie; RDA: Recommended daily allowance; g: gram; AI: Adequate intake; mg: milligram; mcg: microgram.

Table 4. Self-reported dietary behaviour and other nutrition-related indicators by group.

Variable	Controls (n=57)	Mild MS (n=35)	Moderate MS (n=22)	F/χ2 value	*p*-value
DBS (m, SD)	7.6 (1.9)	7.8 (2.2)	8.0 (2.1)	.34	.71
DSES (m, SD)	113.8 (26.8)	114.3 (25.5)	121.8 (26.9)	.68	.50
Specific Diet[a]					
Yes (n, %)	7 (12.2)	7 (20.6)	3 (13.6)	1.2	.55
Gluten free	1 (1.8)	3 (8.7)	0		
Wahls	0	2 (5.8)	2 (9.0)		
Paleo	1 (1.8)	1 (2.9)	1 (4.5)		
Swank	0	2 (5.7)	0		
Other	7 (5.4)	3 (8.7)	1 (4.5)		
Diet Recommendations				9.5	.09
Dietician, Health practitioner	2 (3.5)	4 (11.6)	0		
Other sources[b]	6 (10.8)	6 (17.4)	3 (13.5)		
Nutritional Assessment (n, %)	6 (10.5)	6 (17.1)	7 (31.8)	5.2	.07
Weight Increase					
Increase ≥5% BW (n, %)	6 (10.5)	3 (8.6)	0	3.6	.16
Weight Decrease					
Decrease ≥5% BW (n, %)	4 (7.0)	8 (22.8)	4 (18.2)	7.1	**.03**
Eating Pattern Change					
Yes (n, %)	2 (3.5)	3 (8.5)	3 (13.6)	2.68	.26

Table 4. (Continued)					
Meal preparation (n, %)				7.1	.13
Themselves	45 (78.9)	28 (80.0)	13 (59.1)		
Someone else in the home	7 (12.3)	3 (8.6)	7 (31.8)		
Shared	5 (8.8)	4 (11.4)	2 (9.1)		
Food Security (n, %)				2.1	.34
Always enough to eat of the kinds of foods wanted	47 (82.5)	32 (91.4)	18 (81.8)		
Always enough to eat, but not always the kinds of foods wanted	10 (17.5)	3 (8.6)	4 (18.2)		

[a]Indicates that participants could respond in more than one category. [b]Other sources: family and friends, personal choice, online research. MS: multiple sclerosis; DBS: Dietary Behaviour Scale; DSES: Dietary Self-Efficacy Scale; BW: body weight.

Table 5. Comorbidities, medications, and supplement use by group (n=114).

Variable	Controls (n=57)	Mild MS (n=35)	Moderate-Severe MS (n=22)
Comorbidities	31	14	15
Back pain	14	8	6
Depression	9	8	6
High blood pressure	8	3	7
Osteoarthritis, degenerative arthritis	6	1	5
Diabetes	5	2	4
Anemia or blood disease	4	3	4
Heart disease	4	1	4
Rheumatoid arthritis	4	0	2
Lung disease	3	2	3
Ulcer or stomach disease	2	3	4
Kidney disease	2	1	3
Other (e.g., Thyroid, anxiety, headaches, other)	22	3	2
Medications	13	18	8
Cardiovascular/metabolic	8	7	4
Disease-modifying therapies	-	6	0
Mood	1	5	2
Spasticity	1	5	2
Fatigue/Cognition	0	1	1
Other (e.g., ibuprofen, acetaminophen, other)	7	10	7
Supplements	23	18	13
Minerals			
Calcium	6	6	2
Magnesium	5	7	2
Vitamins			
Vitamin B12	7	9	3
Vitamin B Complex	4	6	3
Vitamin C	3	6	2
Vitamin D	16	13	9
Multivitamin	7	7	3
Lipids	4	9	2
Probiotics	3	9	4
Enzymes	1	7	5

MS: multiple sclerosis.

Chapter 4

Functional and Symptomatic Correlates of Dietary Behaviours in Persons with Multiple Sclerosis

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Preface: This working paper included collaboration between myself, Amanda Gauthier, Dr. Isabelle Giroux, and my supervisor, Dr. Lara Pilutti. Amanda Gauthier and Dr. Isabelle Giroux were consulted with questions specific to dietary intake. This working paper was written by Myriam Venasse and reviewed by Dr. Lara Pilutti.

INTRODUCTION

Multiple sclerosis (MS) is a disorder that is characterized by inflammation, demyelination, and neurodegeneration within the central nervous system (CNS) (1). Persons with MS experience a variety of impairments and symptoms, such as mobility loss, spasticity, visual disturbances, muscular weakness, fatigue, depression, and cognitive impairment (2–11). These impairments and symptoms can limit participation in daily activities and reduce overall quality of life (QOL) (3,12). Currently, there is no cure for MS, and disease-modifying therapies are unable to halt the worsening of disability long-term. As such, lifestyle-based approaches, including diet, for disease management have become increasingly common.

The interplay between diet and MS etiology and progression is likely complex, and currently, this relationship is incompletely understood. There is some evidence for the role of diet in disease activity, disease progression, and disability. Previous research reports that there are links between diets with higher intakes of specific foods (i.e., fruits, vegetables, unsaturated oils) and supplements (i.e., vitamin B12, antioxidants, oil supplements, omega 3 supplements) and reduced disease activity and disability in MS (13–16). Reduced relapse rates have been linked to diets low in fat and high in antioxidants, and in PUFA, fish oil, and vitamin D (17–21). The combination of omega 3 and vitamin D_3 supplementation has been linked with improvements in disability in persons with MS (22). Less is known about potential associations between diet and impairments and symptoms experienced by persons with MS.

There has been interest in the relationship between diet and disease-related outcomes such as function, symptoms and participation in everyday activities. Studies have reported that certain disease-related factors such as fatigue, mobility, pain, and problems with swallowing may increase the difficulty in tasks such as acquiring, preparing, and consuming healthy foods (23,24). Similarly, a study examining risk factors in persons with MS reported that the co-occurrence of insufficient levels of physical activity and poor diet is linked with neuroperformance outcomes (i.e., walking measures) (25). Another study reported that increased intake of fat, decreased intake of

carbohydrates, and increased intake of cholesterol, iron, folate, and magnesium were associated with better ambulation, function, and QOL (26). One study examining vitamin D3 supplementation and depression reported no evidence that this supplementation decreases depressive symptoms (27). Given little evidence in this area, a clear pattern of association has not been established between dietary intake and function, symptomatic, and participatory outcomes in persons with MS.

Self-efficacy (28,29) has been identified as an important predictor of lifestyle behaviours, including diet, across populations. Cross-sectional research examining the role of dietary self-efficacy on dietary behaviours in people with MS has been limited and conflicting. One of these studies reported no relationship between dietary self-efficacy and dietary behaviours (30), while three other studies, conducted with people with MS and in women with physical disabilities, reported a significant relationship between dietary self-efficacy and dietary behaviours (23,31,32). Many factors might influence dietary self-efficacy, including those that are disease-related. One study examining different influences of engagement in health behaviours in persons with disabilities, including MS, highlighted that social support was an important influence of engagement in dietary behaviours (32). Social support has been identified as a predictor of dietary self-efficacy in other populations, such as those with cardiovascular disease (33). Other functional and symptomatic variables, such as fatigue, depression, functional limitations, and neurological impairments are known to influence self-efficacy other health behaviours, such as physical activity, in people with MS (34–36).

Further research examining the relationships between diet, dietary self-efficacy, and other outcomes (i.e., functional, symptomatic, participatory) is necessary. As disease progression in MS is associated with an increased frequency and severity of impairments (37), it would be expected that different factors such as functional, symptomatic, and social influences could impact engagement in dietary behaviours and healthy eating patterns, and this may be influenced through dietary self-efficacy. However, these relationships have not been comprehensively examined in persons with MS. The objective of this study was to examine the relationships among functional,

symptomatic, and participatory outcomes, dietary self-efficacy, and diet in persons with MS using a prospective food intake record. Understanding key factors that are related to dietary intake and behaviours in persons with MS will be essential to identify targets for nutritional interventions in this population.

METHODS

Study design

To examine the relationships between functional, symptomatic, and participatory outcomes, and dietary intake and self-efficacy in persons with MS, a cross-sectional design was used. A sample of 57 persons with MS and 57 age- and sex-matched controls without neurological conditions was recruited. See Figure 3 for a flowchart of participant recruitment.

Participants

Participant recruitment methods are reported elsewhere (See Chapter 3). In brief, participants with MS were recruited through multiple MS-based resources. Controls were recruited through online and local community outlets. Participants were included if they were: (a) between the ages of 18-65; (b) had no history of other neurological conditions; (c) were willing to complete a 3-day diet record and questionnaires. Participants were excluded if they self-reported moderate or severe cognitive difficulty with memory, calculation, or reasoning through the self-reported EDSS scale (38). Controls were matched to participants with MS based on age and sex.

Outcome measures

Demographics and health history. Participants completed a demographics questionnaire. Self-reported height and weight were used to calculate body mass index (BMI, kg/m^2). BMI was categorized as underweight, BMI<18.5kg/m^2; normal weight, BMI=18.5-24.9kg/m^2; overweight, BMI=25.0-29.9kg/m^2; and obese, BMI≥30.0kg/m^2, as per standard values (39).

Neurological disability status. Neurological disability level in persons with MS was assessed using the Patient Determined Disease Steps (PDDS) scale. The PDDS is a self-reported measure of neurological disability that correlates strongly (r=.93; ρ=.783) with the clinically-administered Expanded Disability Status Scale (40).

Diet

Dietary intake. A 3-day food intake record was used to assess dietary intake in both persons with MS and matched controls. Participants were provided with an instruction sheet with information on how to record their dietary intake using an electronic or paper spreadsheet. Instructions included how to measure food (i.e., using measuring utensils such as spoons and cups) as well as a sample day to provide an example of what information was required on the food intake record. The food intake records were completed within a 7-day period including two week days and one weekend day. Food intake record data were entered and analyzed using ESHA The Food Processor (Salem, Oregon).

Dietary behaviours. Participants completed a 5-item overall dietary behaviours scale, indicating whether they rarely, sometimes, or often engaged in specific dietary behaviours, such as making good food choices, eating 5 servings and fruits of vegetables per day, limiting fat intake, reading labels, and eating regularly. Scores on this scale range from 0-10, with a higher score indicating engagement in healthier dietary behaviours.

Dietary self-efficacy. Dietary self-efficacy was measured using a combination of two individual scales. First, a 5-item scale assessing confidence (from 1=not at all to 10=completely) for engaging in dietary behaviours (i.e., eating a well-balanced diet, following a diet recommended by your doctor, selecting foods that will help you maintain weight, selecting appropriate vitamins and supplements, and identifying nutrients by reading food labels). This scale has been used in the MS population and with other physical disabilities (32), and was built through studies of other chronic diseases (41,42). Dietary self-efficacy was also measured using 10 of the 16 items from the Cardiac Diet Self-Efficacy Scale (CDSES), a more general measure of dietary self-efficacy

assessing levels of confidence (from 1=very little to 5=quite a lot) for engaging in healthy dietary behaviours (43). This scale has not been used in the MS population.

Physical and Cognitive Impairment

Walking impairment. The 12-item MS Walking Scale (MSWS-12) (44) was used to assess the impact of MS on walking (from 1 = not at all to 5 = extremely) in the past two weeks. The total MSWS-12 score ranges from 0 to 100, where higher scores indicate a greater impact of MS on walking.

Cognitive impairment. The Perceived Deficits Questionnaire (PDQ) was used to measure activity limitations due to cognitive impairment. It includes 5 items for which participants must rate how often they experience difficulties with specific activities on a 5-point scale (from 0-never to 4-always). Higher scores indicate greater cognitive impairment.

Symptoms

Fatigue. Fatigue was measured using the Modified Fatigue Impact Scale (MFIS) (46), which is composed of 3 subscales: physical, psychosocial, and cognitive. This scale assesses how daily activities are impacted by fatigue due to MS (from 0 = never to 4 = almost always) over the preceding month. A higher total score indicates a greater impact of fatigue on daily activities.

Anxiety and Depression. Symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) (47), which is composed of two subscales: anxiety and depression. For each item, participants reported the frequency of those feelings over the past four weeks (from 0 = not at all to 3 = most of the time). Higher scores indicate a greater frequency of anxiety and depressive symptoms.

Participatory

Social support. Perceived social support was measured using the Medical Outcomes Study Social Support Survey (MSSS) (48). The MSSS is used to measure five dimensions of social support (emotional support, informational support, tangible support, positive social interaction, and affectionate support), and 2 items identifying the number of persons providing social support.

Participants reported how often (1 = none of the time, 5 = all of the time) different types of support were available if they needed it. A higher score indicates a greater frequency in availability of each specific type of social support.

Activities of Daily Living. Functional limitations in everyday life were measured using the Late Life Function and Disability Instrument (LLFDI) (49). The LLFDI includes a disability component and a functional limitations component. In the disability component, participants indicate how often they how often they do an activity (5 = very often, 1 = never), and the extent that they feel limited in the activity (5 = not at all, 1 = completely). Lower scores indicate greater disability or functional difficulties with performing everyday tasks. The functional limitations component of the LLFDI contains 15-items within three subscales: upper extremity function, and basic and advanced lower extremity function. For each item, participants indicate how much difficulty they have doing specific activities (5 = none, 1 = cannot do). The composite score is generated by summing all three subscale scores. Higher scores indicate fewer functional limitations in activities of daily living.

Procedures

Interested individuals contacted the research team to receive more information about the study. All participant screening was conducted over the telephone with a checklist of criteria for inclusion and exclusion. Participants who were eligible received study materials, including a consent form and study packet with instructions and study materials, through the mail or email. Each participant was contacted a few days after the materials were distributed to review the consent form and instructions. Participants were asked to complete all study materials within one week. Once the materials were received by the research team, all data were checked for completeness and participants were contacted to verify missing responses. Participants were compensated with a $15 gift card and were provided a handout containing information on diet and nutrition and resources to consult for more information.

Data analysis

IBM SPSS Statistics Version 25.0 (Armonk, NY) was used to complete all data analyses. Descriptive statistics were used to characterize demographic and clinical characteristics of the sample. Bivariate Spearman correlation coefficients (ρ) were used to examine the relationships among dietary intake, dietary self-efficacy, impairments, symptoms, and participatory outcomes. The magnitude of the correlation coefficients were interpreted as small, moderate, and large, based on effect sizes of 0.1, 0.3, and 0.5, respectively, using Cohen's criteria (50). Values are presented within the text as mean (SD), unless otherwise noted.

RESULTS

Demographics

Demographic characteristics for MS and control groups are presented in Table 1. There were no significant differences in age (m=47.7 and 48.8) and sex (approximately 80% female) between groups. There were significant differences in employment status between groups, where significantly more persons with MS were unable to work due to illness or disability. There were no significant differences in education, height, weight, or BMI between groups. The mean disease duration for the MS sample was 13.6 years (9.6). Overall, the sample consisted of more persons with RRMS (66.7%) than persons with progressive types of MS (29.8%). The median (interquartile range) PDDS score was 2.5 (2.0), indicating that the sample involved persons with mild disability who experienced some difficulty with walking, but did not require an assistive device, and experienced some issues with MS that are impacted their daily activities.

Correlations

Correlation coefficients among functional, symptomatic, participatory, and dietary intake and behaviour variables are reported for the MS group (Table 2) and the control group (Table 3).

Dietary intake and behaviours

In the MS group, there was a significant correlation between walking and folate intake (ρ= -.34, p=.009). There were significant relationships between fatigue and the intake of vitamin A (ρ= .27, p=.04), and folate (ρ= -.34, p=.009). There was a significant relationship between depression and the intake of vitamin C (ρ= -.29, p=.03) and overall dietary behaviours (ρ= -.27, p=.03), and between anxiety and the intake of vitamin A (ρ= .28, p=.03), sodium (ρ= .31, p=.02), and magnesium (ρ= .27, p=.04). There was a significant relationship between social support and protein intake (ρ= -.36, p<.001).

In the control group, there were significant relationships between anxiety and folate intake (ρ= .29, p=.03), and between social support and magnesium intake (ρ= .28, p=.03). There were no other significant relationships between functional, symptomatic, and participatory outcomes and other intake variables.

Dietary self-efficacy

Correlations among dietary self-efficacy with dietary intake, behaviours, and other functional and symptomatic variables are reported here. In the MS group, there were significant relationships between dietary self-efficacy and cholesterol (ρ= -.29, p=.03), vitamin C (ρ= .32, p=.02), and sodium (ρ= -.32, p=.01) intake, and overall dietary behaviours (ρ= .38, p=.003). Dietary self-efficacy was related to cognition (ρ= -.32, p=.01), depression (ρ= -.42, p=<.001), anxiety (ρ= -.29, p=.03), and social support (ρ= .37, p=.005).

In the control group, dietary self-efficacy was not related to any dietary intake variables from the 3-day intake record. There was a significant relationship between dietary self-efficacy and overall dietary behaviours (ρ= .64, p<.001). Dietary self-efficacy was further related to depression (ρ= -.33, p=.01), anxiety (ρ= -.41, p<.001), social support (ρ= .32, p=.01), and activities of daily living (ρ= .30, p=.02) in controls.

DISCUSSION

The present study sought to examine the relationships among functional, symptomatic, and participatory outcomes, dietary self-efficacy, and diet in persons with MS. Our results indicate MS-specific associations between functional, symptomatic, and participatory variables and dietary intake. Dietary self-efficacy was associated with overall dietary behaviours in persons with MS and controls, but with few specific macro- or micronutrients, based on food intake records. Dietary self-efficacy was related to many and similar functional, symptomatic and participatory variables in persons with MS (cognition, depression, anxiety, and social support) and in controls (depression, anxiety, social support, and activities of daily living). Collectively, this suggests that there are specific factors with a relationship to dietary self-efficacy that would make interesting targets in future dietary interventions with persons with MS.

Dietary intake

There were more significant relationships observed between dietary intake variables and functional, symptomatic, and participatory outcomes in the MS group, when compared to the control group. In the present study, a significant relationship between walking and folate intake was observed, which matches the results of a recent study that reported a significant negative correlation between folate and walking using the 6-Minute Walk Test (6MWT) and the Timed 25-Foot Walk Test (26). There were significant relationships between fatigue and vitamin A and folate intake in the current study. The relationship between fatigue and folate has been reported in previous research in MS (51). Lower levels of folate have previously been reported in people with MS compared to controls without MS (52). Folate plays important roles in immune and nervous system functions, and low levels of folate can lead to oxidative stress, DNA destruction and mitochondrial dysfunction (53). There were significant negative associations between depression and vitamin C in the current sample, and these relationships have not been previously explored in people with MS. Previous studies have reported no significant relationships between dietary intake (i.e., 24-hour food recall) and depression in older adults (54), and others have reported

significant relationships between dietary intake (i.e., dietary screening tool), and depressive symptoms in older adults (55). There were significant relationships between anxiety and vitamin A, sodium, and magnesium in people with MS. These relationships have not been reported in persons with MS.

Dietary self-efficacy

In the MS group, there was a significant positive relationship between overall dietary behaviours and dietary self-efficacy. Similar studies in persons with MS, and in women with disabilities, have identified dietary self-efficacy as the strongest predictor of dietary behaviours among physical, psychological, social, and environmental variables (31,56). However, the present study found that there were few, significant relationships between dietary self-efficacy and dietary intake based on the 3-day food record. These results match findings presented in previous research in women with MS, in which only age and depression had a significant relationship with dietary intake variables (30). This suggests that there are likely differences in what the Dietary Behaviours Scale and the food intake record are capturing, and how these variables correspond with dietary self-efficacy. This may be attributed to the 5-item dietary self-efficacy questionnaire and the 5-item Dietary Behaviour Scale reflecting more general aspects of diet and diet-related choices than the food intake record, which provides specific of nutrient intake (31). While there were some relationships between dietary self-efficacy and specific micronutrients from the 3-day food record (i.e., cholesterol, vitamin C, and sodium), there were no associations with the macronutrients. This could be attributed to the specific items of the Dietary Self-Efficacy Scale (i.e., identifying nutrients by reading food labels, selecting foods that help maintain weight, increase the amount of fibre and vegetables in your diet, etc.), which could perhaps be reflected in dietary intake through less sodium and cholesterol intake, and more vitamin C intake. The finding of a significant relationship between overall dietary behaviours and dietary self-efficacy in the control group is supported by previous literature reviews, in which dietary self-efficacy was

often found to be associated with dietary change behaviours and nutrition in the general population (57).

There were similar significant relationships between dietary self-efficacy and other functional, symptomatic, and participatory variables (i.e., depression, anxiety, social support, and activities of daily living) in the MS group and in the control group. In the MS group, lower levels of self-efficacy were associated with greater cognitive impairment, and symptoms of depression and anxiety, but not fatigue. Research examining diet quality, disability, and symptom severity in MS reported that individuals who engaged and continued to maintain a healthier lifestyle (i.e., including diet) had a lower prevalence of cognitive symptoms, fatigue, and depression (58). To our knowledge, there are no studies in persons with MS that have reported on the association between dietary behaviours and depression. Previous research examining associations between depression and dietary intake in the general population have found conflicting evidence for this association (13).

As reported in previous research, there was no significant association between dietary self-efficacy and walking (31). To our knowledge, previous research has not explored the relationship between dietary self-efficacy and activity limitations. It is possible that activity limitations might follow similar patterns as walking and neuroperformance outcomes, such that there may be a relationship between high levels of activity limitations and poor dietary self-efficacy. However, this was not observed in the present study. Some previous research examining dietary intake in an MS sample reported no relationship between dietary self-efficacy and social support (30), while another study of women with disabilities including MS did report a significant positive association between these variables (56), similar to the present study. The relationship between social support and dietary self-efficacy has been previously established in populations with other diseases (i.e., cardiovascular), but has not been established in MS (33).

Collectively, these data identify that multiple symptoms and impairments, such as cognition, depression, anxiety, and social support have a relationship with specific micronutrients

and dietary self-efficacy in persons with MS. Given the cross-sectional nature of this study, the potential direction of these associations is unclear at this time. It is possible that certain symptoms or impairments are leading to changes in the diet of persons with MS, or that certain dietary patterns are contributing to symptoms and impairments. This suggests that there is potential for future interventions in persons with MS that target symptoms and impairments or dietary intake to have some benefits in persons with MS. Dietary self-efficacy was further related to overall dietary behaviours, but not to the intake of specific nutrients. This suggests that certain symptoms and impairments may become targets in future dietary interventions to increase dietary self-efficacy and overall behaviours in persons with MS, whereas anxiety and social support may be better targets for these dietary interventions in the general population. These relationships require further investigation in large samples to determine the directionality of associations and the contribution of self-efficacy as a mediator of dietary behaviours.

This study has limitations. All data collected were self-reported, yet scales used in this study were often used in MS studies, were validated, and show good psychometric properties. Persons with MS and matched controls who have limited interest in dietary behaviours may not have been interested in study participation. This sample might not be representative of the MS population, and of the general population. We attempted to counter this by distributing recruitment materials broadly and ensuring that the study was available online and in paper form. Another limitation is the cross-sectional design of this study which limits causal inference, as previously discussed.

In conclusion, dietary self-efficacy was identified as being significantly associated with overall dietary behaviours in persons with MS and matched controls, but was related to few specific macro- or micronutrients. Symptoms and impairments such as walking, fatigue, and anxiety were identified as having relationships with dietary intake in persons with MS. This work identifies dietary self-efficacy and some aforementioned variables as preliminary targets for future nutritional interventions in persons with MS, and provides direction for next steps in this research.

Large studies are required to understand how dietary self-efficacy, function, symptoms, and participatory outcomes impact nutrition in persons with MS, and to identify additional targets for nutritional interventions in this population.

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Chapter 4

Tables

***Table 1*.** Demographic and clinical characteristics for all participants. Values are reported as means and SD, unless specified otherwise.

Variable	Controls (n=57)	MS (n=57)	t/χ2 value	*p*-value
Age (years)	47.7 (11.0)	48.8 (10.2)	-.53	.59
Sex (% female)	82.5	80.7	.24	.81
Height (cm)	166.6 (8.4)	167.3 (8.3)	-.42	.67
Weight (kg)	74.6 (17.8)	72.7 (18.9)	.27	.78
BMI (kg/m^2)	26.8 (5.7)	25.9 (6.4)	.43	.67
Education (n, %)			7.3	.12
Partial high school	0	3 (5.3)		
High school	7 (12.3)	7 (12.3)		
College	9 (15.8)	17 (29.8)		
Bachelor's degree	27 (47.4)	21 (36.8)		
Master's or higher	14 (24.6)	9 (15.8)		
Employment (n, %)			28.8	**<.001**
Employed	50 (87.7)	25 (43.9)		
Unemployed	2 (3.5)	2 (3.5)		
Retired	4 (7.0)	8 (14.0)		
Unable to work due to illness or disability	1 (1.8)	22 (38.6)		

MS: multiple sclerosis; cm: centimetre; kg: kilogram; m: metre; BMI: body mass index.

Table 2. Functional and symptomatic correlates of dietary intake in persons with MS.

Variable	Walking	Cognition	Fatigue	Depression	Anxiety	Social support	Activities of daily living
Energy intake	-.07	.02	-.13	.10	.19	-.18	-.13
Protein	-.07	.15	-.03	.002	.20	-.36**	-.01
Fat	.01	-.04	.04	.20	.22	-.12	-.12
Saturated fat	.22	-.10	.07	.13	.23	-.07	-.18
Carbohydrates	-.14	.01	-.16	.06	.12	-.20	-.04
Fibre	-.03	.17	.02	.12	.22	-.15	-.05
Cholesterol	-.02	.05	.02	.15	.09	-.21	-.12
Omega 3	-.10	.01	-.05	-.06	.19	-.03	.01
Vitamin A	.09	.17	.27*	.03	.28*	-.13	.10
Vitamin B12	-.03	.08	.10	-.03	.18	-.09	-.04
Vitamin C	-.16	.17	-.10	-.29*	.13	-.01	.07
Vitamin D	.15	-.05	.26	.01	.22	-.11	-.17
Calcium	-.16	-.003	.002	.16	.15	-.17	-.06
Sodium	-.15	-.01	.03	.23	.31*	-.19	.09
Folate	-.34**	-.15	-.34**	-.18	.12	-.02	.18
Iron	-.12	.002	-.06	-.01	.05	-.18	.05
Magnesium	-.12	.10	.08	.05	.27*	-.15	.10
Manganese	-.14	.06	-.002	-.03	.15	-.11	.06
DBS	-.13	.07	-.07	-.27*	-.10	.17	-.001
Mean	39.55	22.24	33.02	5.74	5.16	75.82	54.10
SD	36.75	14.36	16.83	3.72	3.50	23.80	19.08

MS: multiple sclerosis; Walking: Multiple Sclerosis Walking Scale (MSWS); Cognition: Perceived Deficits Questionnaire (PDQ); Activities of Daily Living: Late Life Function and Disability Instrument (LLFDI); Anxiety: Hospital Anxiety and Depression Scale (HADS); Depression: Hospital Anxiety and Depression Scale (HADS); Fatigue: Modified Fatigue Impact Scale (MFIS); Social Support: Medical Outcomes Study Social Support Survey (MSSS); Dietary behaviours: Dietary Behaviours Scale (DBS).

Table 3. Functional and symptomatic correlates of dietary intake in matched controls.

Variable	Cognition	Depression	Anxiety	Social support	Activities of daily living
Energy intake	-.06	-.11	-.07	-.001	-.05
Protein	-.10	-.14	.02	.14	.12
Fat	.04	-.03	-.06	.03	-.02
Saturated fat	.02	-.02	-.13	.03	-.13
Carbohydrates	-.01	-.12	-.14	-.04	-.03
Fibre	-.07	.06	.02	-.10	.07
Cholesterol	.04	.11	.02	-.24	-.10
Omega 3	-.03	-.19	-.01	.07	.07
Vitamin A	-.02	.03	.07	-.02	.21
Vitamin B12	.07	.07	.18	.24	.06
Vitamin C	-.01	.02	-.02	.02	.19
Vitamin D	-.12	.13	.06	.25	.22
Calcium	-.18	-.22	-.04	.08	-.06
Sodium	.10	.12	-.02	-.04	.06
Folate	.06	.07	.29*	.01	.06
Iron	-.23	-.01	-.17	.01	.10
Magnesium	-.01	-.006	.19	.28*	-.003
Manganese	-.14	-.09	.10	.05	-.07
DBS	-.13	-.097	-.18	.07	.19
Mean	13.65	3.44	4.52	81.91	68.36
SD	8.63	3.67	3.38	21.32	10.97

Cognition: Perceived Deficits Questionnaire (PDQ); Activities of Daily Living: Late Life Function and Disability Instrument (LLFDI); Anxiety: Hospital Anxiety and Depression Scale (HADS); Depression: Hospital Anxiety and Depression Scale (HADS); Social Support: Medical Outcomes Study Social Support Survey (MSSS); Dietary behaviours: Dietary Behaviours Scale (DBS).

Chapter 5

Discussion and Conclusion

5.1 INTRODUCTION

Despite increased interest in wellness and MS, most research that has been conducted in this field includes few studies with persons with MS with higher disability scores and progressive disease courses. This is a key limitation considering that approximately half of persons with MS have a progressive diagnosis (1) and disability progression cannot be halted using current disease modifying therapies (2). Further, very few studies have examined dietary intake in this population using high-quality methodologies. To date, little is known about the efficacy of wellness interventions in persons with progressive MS, and about how disability affects nutritional status among persons with MS. This thesis examined wellness behaviour interventions in persons with progressive MS, dietary intake in persons with MS, and functional and symptomatic correlates of dietary behaviours in persons with MS. First, the review focusing on wellness interventions aimed to investigate the efficacy and feasibility of wellness interventions in persons with progressive MS. The results from this review identified that most interventions that have been conducted are generally of low quality, but that some interventions show promising results. Therefore, it is difficult to make conclusive recommendations regarding wellness interventions for persons with progressive MS at this time. Further, high-quality studies are required in order to be able to determine the feasibility and efficacy of wellness interventions for persons with progressive MS.

The interest in wellness behaviours has not only been seen in research studies, but has also been expressed by persons with MS. Given the interest of persons with MS in behaviours such as diet, and the lack of research investigating dietary intake in persons with MS based on disability status, we characterized dietary intake in persons with MS across a variety of disability levels, and with a matched control sample for comparative purposes. As there are few studies examining correlates of diet in persons with MS, we also examined correlates of dietary behaviours in persons with MS and matched controls. These correlates included functional and

symptomatic factors that could impact dietary behaviours and might become targets of dietary interventions.

5.2 WELLNESS REVIEW

The wellness review conducted as part of this thesis examined 21 articles reporting on 16 studies that contained wellness-based interventions for persons with progressive MS. Ten of these trials were exercise training interventions, three were emotional therapies focusing on wellness, two involved dietary modification, and one trial was a combined intervention (3). The American Academy of Neurology criteria were used to assess the level of evidence for each trial (4). Overall, when looking at the dietary modification trials specifically, there was a lack of evidence for the efficacy of these interventions in persons with progressive MS (3), and in MS overall (5,6). It is not possible to definitively support dietary interventions in persons with MS, regardless of the disease course (i.e., RRMS, PPMS, SPMS), given the conflicting results that have been reported (5,6). High-quality studies are required to be able to determine which dietary interventions are most effective in this population, by disability status, and by disease course (3). Also, increasing characterization regarding wellness behaviours, such as diet in persons with MS with different levels of disability and with different disease courses will be a key part in designing future high-quality interventions (3).

5.3 CHARACTERIZING DIETARY INTAKE IN MS

Currently, there is a lack of DRI recommendations specific to persons with MS. Some dietary recommendations that are commonly made by researchers and health professionals for persons with MS include diets that are balanced, low in fat, and high in fibre (7,8). Supplementation recommendations that are strongly supported include vitamin D and omega-3 fatty acids (8,9). In the present study sample, 17.5% of individuals with MS reported following a specific diet; however, few of these individuals (7%) with MS had consulted with a Registered Dietician. As the

recommended daily intake for most nutrients were either not met or were exceeded, and as there are many other comorbidities in this sample that may affect nutritional status, it is important to encourage persons with MS to consult with a Registered Dietician or another healthcare practitioner before making dietary changes (10). These consultations could act as preventative measures to avoid the development of potential nutritional deficiencies and diet-related comorbidities (i.e., cardiovascular, metabolic) in the future for these individuals.

Given the lack of MS-specific DRI recommendations or dietician consultations, it is possible that people with MS are seeking online or other sources for dietary recommendations to help manage their MS. Recent studies have reported that persons with MS often consult the internet for information on their MS before speaking with their healthcare provider (11). In a sample of 8656 North American Research Committee on Multiple Sclerosis (NARCOMS) participants, just under half of online searches by persons with MS were regarding complementary and alternative therapies, such as diet (11). These results demonstrate that persons with MS desire and are willing to make dietary and lifestyle modifications to improve their disease. However, the websites that are consulted for this information may not present accurate information, might not include references to support their claims, and might also be presenting information that is conflicting with that of other sources (10). The information presented on these websites may lead to the intake of a variety of supplements and/or dietary modifications, for which there is very little evidence, as previously explained (3,5,6). It is important to consider that the information presented on some websites might be ineffective, costly, or perhaps detrimental to the health of persons with MS who chose to follow these recommendations (10). This points to the need for further research examining the desire and willingness of persons with MS to make dietary of lifestyle modifications. Further, additional research examining the efficacy of dietary interventions, including supplement use in persons with MS is required, and also for ensuring that this information is disseminated to persons with MS primarily through communication with physicians or other healthcare providers. This will allow physicians and healthcare providers to direct their patients to sources that are

considered to be credible (i.e., the MS Society and other government-affiliated organizations), or to refer them to Registered Dieticians for consultation, when necessary (10).

As for disability and diet, there were not many differences in dietary intake or behaviours based on disability status. It was expected that persons with MS with higher disability levels would have poorer dietary intake when compared to persons with MS with lower disability levels, and when compared with controls without MS. This was expected as persons with MS with higher disability may be facing additional challenges (i.e., decreased mobility, difficulty acquiring food and preparing food) (12) to engaging in healthy dietary behaviours. Most differences found between the MS and control groups seemed to be attributed to use of supplements among persons with MS. In this sample, although there were no significant differences in meal preparation across groups, there were more persons with MS with higher disabilities that reported that someone else did the cooking at home. Persons with MS with higher disability levels may have specific strategies that ensure an adequate dietary intake when they are unable to acquire food (i.e., food delivery service) or when they are unable to participate in meal preparation due to MS symptoms (i.e., with the support of a caregiver). It is also possible that there were not many differences between disability groups as there were few participants at the higher end of the disability spectrum, and the moderate-to-severe disability group was smaller than the mild disability group. Further research examining these strategies is required to understand which factors are barriers and facilitators to the engagement in dietary behaviours of persons with MS across levels of disability. For example, a qualitative study of nutritional behaviours of adults with MS identified that the physical and social environments play important roles in their influence of nutritional behaviours, but that the social environment might be the best target for future nutritional interventions in this population as family dynamics can play either a positive or negative role in nutritional behaviours (12).

5.4 CORRELATES OF DIETARY BEHAVIOURS IN MS

The second paper presented functional and symptomatic correlates of dietary behaviours in persons with and without MS. The differences in correlations that were observed between these two groups indicated that the factors that influence dietary intake in persons with MS and in the general population may be different. These differences identify that factors such as dietary self-efficacy and multiple symptoms and impairments, such walking, fatigue, and anxiety may be important targets in future dietary interventions with persons with MS, whereas anxiety and social support may be better targets for dietary interventions in the general population. It should be noted that it was not possible to complete a regression analysis for the second paper as initially intended. It was expected that, as depicted in Figure 1, there would be relationships between different factors and dietary self-efficacy, and between dietary self-efficacy and dietary intake, specifically the macronutrient intakes. The data that were collected did not support to our original hypothesized model based on SCT, and the relationships found between variables did not make it possible to complete these regression analyses. Most correlations that existed between functional, symptomatic, and participatory outcomes and specific nutrients were with micronutrients, and this made the data difficult to interpret with regression analyses. While SCT has been successfully applied to explain other health behaviours in the MS population (13), this theoretical approach may not be suitable for explaining dietary behaviours in persons with MS. The variables that were examined in this study were chosen based on their expected relationship with SCT constructs. Perhaps there are other variables, such as physician communication, self-management (14), or other theoretical models, that were not examined in the context of this study and that should be examined in future research.

5.5 LIMITATIONS

There are potential limitations of this research that require consideration. An important limitation of this project is that the data was self-reported. However, most scales that were used for this project have been validated against clinically-administered scales and also show good

psychometric properties. A limitation pertaining to the theoretical model that we chose was that the full sociocognitive causal structure was not used. Certain factors, such as personal goals, were not explored as part of this study. This may have led to our inability to conduct a regression analysis. Another limitation is that dietary intake can be challenging to assess. For example, participants may have over- or underreported consumption of certain types of foods, such that participants might have reported healthier dietary intake or altered their diet consumption during the monitoring period. Studies have reported that using a food intake record can alter eating behaviours through self-monitoring and social desirability bias (15). We attempted to limit this effect by explaining the food intake record to participants in detail, ensuring that they understood the detailed written instructions, and by telling them to report as honestly as possible. Participants were asked to complete the log for 2 weekdays and 1 weekend day, and were asked to maintain their usual dietary intake, and to avoid days with irregular eating patterns (e.g., holidays). The 3-day food intake record can also have high participant and researcher burden (15). However, a 3-day food intake record allowed for prospective, quantitative dietary intake without requiring subject recall. It would be interesting to have the same individuals complete multiple 3-day food intake records over multiple time points to be able to evaluate longitudinal changes in dietary behaviours. Data collection lasted approximately one year, which means that the dietary intake was not affected by seasonal variations in food availability and selection. Another potential limitation is that respondents with little interest in dietary habits may have been less likely to participate in this study. Therefore, the sample might not be representative of the general MS population. We attempted to limit this effect by dispersing recruitment materials as broadly as possible and by making the study accessible by providing multiple avenues for completion (i.e., online and print). Further, data were collected only at one-time point; therefore, dietary habits over time were not be examined.

5.6 FUTURE DIRECTIONS

As indicated through the systematic review, there is a lack of high-quality wellness intervention studies in persons with progressive MS. The current literature in this field is very limited, particularly with respect to dietary interventions, and there is a multitude of gaps in the field that require attention in order to build a greater understanding of the benefits and the efficacy of wellness interventions for persons with progressive MS. There is a demand for more of these interventions by researchers, health care providers, and members of the public. Determining which interventions will be the most effective will require multiple RCTs of high quality, including persons with MS with severe disability. Greater attention should be given to the proportion of MS subtypes within the sample, as well as to the disability level of the sample. Given the limitations that persons with MS with higher disability levels may experience with transportation and accessibility to research sites, the delivery methods of dietary interventions should include innovative strategies to encourage participation of individuals with greater disability. These strategies could include Internet-delivered or telephone-delivered programs directly within the home, and the use of a food delivery services. These approaches have been effective for the modification of other health behaviours, such as physical activity (16,17) in persons with MS.

5.7 CONCLUSION

This thesis provided a comprehensive and much needed perspective on the relationship between disability and dietary patterns in people living with MS. The characterization of dietary intake provides important information for patients and healthcare practitioners about potential alterations in overall and specific dietary outcomes that might be expected among people with MS, particularly with respect to disability status. Health care professionals can expect that persons with MS face different challenges than persons in the general population, and that these individuals might be modifying their diets and taking supplements. This information may help to guide targeted interventions for improving dietary intake and status in people with MS. This study further identified potential modifiable variables associated with dietary intake in people with MS,

including dietary self-efficacy, walking, fatigue, depression, anxiety, and social support. The identification of disease-related factors that are related to dietary patterns is important to design effective behavioural interventions for improving nutritional status in people with MS. Further research is required to understand how disability and disease progression influences dietary intake and eating patterns in persons with MS, and to identify targets for future nutritional interventions in this population.

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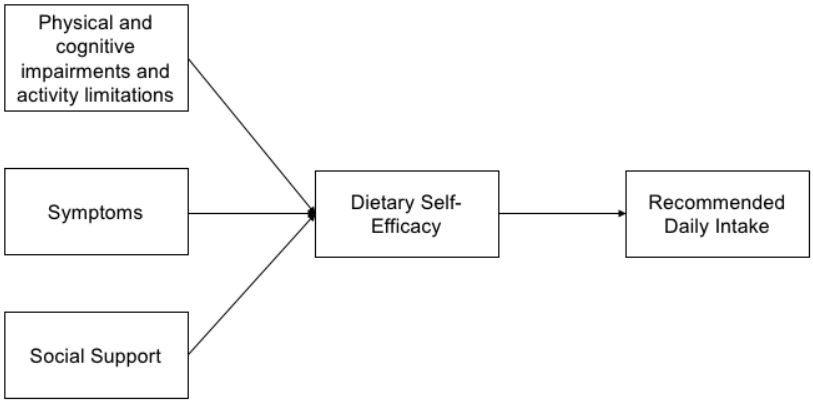
Chapter 5

Figures

Figure 1. Hypothesized relationships among factors that directly or indirectly influence RDI. RDI; recommended daily intake.



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CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

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Statut du projet / Project Status	Approuvé / Approved
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